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Pathogenesis of Pulmonary Tuberculosis.—Examination of aerodynamic phenomena of respiration has shown that there are two traumatizing phases, one during inspiration, the other at the end of the inspiration. These traumatizing phases are due to the energy that inhaled air acquired during inspiration; this energy is due to the sudden difference between external and intrapulmonary pressures. Under normal conditions the bronchial musculature, possessing such energy in itself, regulates the air passage so that contact between inhaled air and functional elements is very gradual; in the alveoli, however, there is positive pressure at the end of inspiration, which challenges their elasticity. These phenomena are necessary for the gaseous exchange. When a pathological process, such as pulmonary tuberculosis or any other pulmonary disease, has damaged the bronchial musculature and has lowered the elastic powers of the alveoli, inhaled air traumatizes those functional elements that are already in a lowered condition of resistance, and the damage to these bronchi and alveoli is proportional to the power behind the column of inhaled air. The mechanical factor that acts together with other factors in the pathogenesis of pulmonary tuberculosis and of other pulmonary disease processes is generally constituted by the energy with which the air enters the lung. If we accept this interpretation, the therapeutic problem consists in the reduction in the sudden difference between external and intrapulmonary pressures at the time of inspiration. Good clinical results proportional to the amount of reduction in this difference have been noted either when patients were brought to higher altitudes, or when they had been subjected to collapse therapy.—*Nuovi concetti sul fattore meccanico nella patogenesi della tuberculosi pulmonare, L. Menozzi, Lotta contro la tuberc., December, 1939, 10: 998.—(S. L.)*

Haemoptysis.—This paper is concerned with observations regarding the branch of the pulmonary artery which appears to be the cause of fatal haemoptysis. Twelve cases of fatal haemoptysis in pulmonary tuberculosis were studied clinically, pathologically and by post-mortem arteriography. The disease in all cases was chronic with considerable fibrosis. The ruptured pulmonary artery was demonstrated in 10 of 12 cases. In 2 it was not found, but it is quite certain that the fatal haemorrhage occurred in a cavity in the upper lobe. In 8 of the 10, the ruptured vessel was the first main branch of the pulmonary artery which lies at the level of the second costal cartilage slightly medial to the parasternal

line. There are two reasons for this artery being involved. The first lies in the fact that in pulmonary tuberculosis of the adult type with disease chiefly in the upper lobe it is the first branch of the pulmonary artery supplying that area that bears the brunt of the pathological process. In the chronic type of disease the artery in the diseased area becomes sclerosed and the lumen almost obliterated, while the remainder of the vessel remains normal in size or becomes dilated. In the acute type of disease the vessel is narrowed throughout the consolidated area. But regardless of the type of disease, this is the arterial vessel most frequently destroyed. The second reason for haemorrhage occurring more frequently from this vessel lies in the fact that tuberculous cavities usually begin in the apex and involve the ends of the first branch. When a cavity is not more than one inch in diameter and does not extend below the second rib, only the second and third order of this vessel are eroded. Probably few fatal haemorrhages occur from these vessels. A cavity reaching the second costal cartilage or below may well be considered as dangerous as far as possible erosion of the first main branch is concerned. Hence the collapse of such a cavity is to be seriously considered.—*Hemoptysis and Pulmonary Arterial Rupture, R. Charr & J. W. Savacool, Am. J. M. Sc., May, 1940, 199: 641.*—(*G. F. M.*)

Tuberculous Cavities.—Existing theories on the pathogenesis of excavation in pulmonary tuberculosis are reviewed, with emphasis on the part played by the draining bronchi. Spontaneous healing is rare and pneumothorax, applied in an early stage, is most important in treatment. The expectant attitude, adopted in many dispensaries, leads to serious consequences.—*Cavernas, Mecanismos de produccion, Clasificación, Evolución, Curación, G. A. Espinosa Nodal, Rev. Mexicana de Tuberc., April, 1940, 2: 63.*—(*E. R. L.*)

Tuberculosis in Older Ages.—In a period of five years 1,143 autopsies were performed on tuberculosis patients at Sea View Hospital and 380 of these were in individuals over forty years of age at the time of death. Three hundred and thirteen of the patients over forty were white, 63 were Negroes and 4 were of the yellow race. This is in marked contrast to the ratio of 7 white to 4 Negroes which is found in all ages. Of the 380 patients, 216 had been ill less than two years. In 7 cases the lungs were clear except for a healed primary complex. Five had healed chronic pulmonary tuberculosis, 10 old haematogenous foci and in 16 generalized miliary tuberculosis was found. Chronic pulmonary tuberculosis was present in 328 cases and 13 of these had had a terminal miliary dissemination. In 105 (32 per cent) the process was described as old or benign on the basis of the pathological process discovered. One hundred and ninety-two (59 per cent) were classed as moderate, a form comparable to the vast majority of cases between twenty and thirty-nine years of age. Only 31 cases (9.4 per cent) had an acute or fresh type of tuberculosis. There is thus a marked decrease in the number of acute cases in the older ages. Twenty-two had had a rupture of a branch of the pulmonary arteries and this very high incidence is attributed to the increase in the number of chronic cases above the age of forty years. Fifteen had bronchopleural fistulae. Far advanced silicosis was found in 21 of the 380 cases and of these 20 had chronic pulmonary tuberculosis and one had generalized miliary tuberculosis. Eight cases had associated carcinoma of the lung. Laryngeal tuberculosis was found as frequently above the age of forty years as below this age. However, intestinal tuberculosis was found much less frequently. Tuberculosis of the skeletal system occurred in 11.6 per cent of this group and of the urinary system in 6.8 per cent. Diabetes was found in 35 cases and heart disease in 71. Pneumothorax had been attempted in 58 cases, 49 of which died within two years after the institution of pneumothorax. Thoracoplasty was performed in 13 patients and in only one of these was the sputum rendered negative. In 265 of the 380 cases tuberculosis was considered the cause of death; the remainder died of heart disease, fatal pulmonary haemorrhages, cerebral accidents and uraemia.—*The Pathology of Tuberculosis in the Older Ages, O. Auerbach & H. Green, Quart. Bull. Sea View Hosp., April, 1940, 5: 237.*—(*A. A. E.*)

Experimental Bronchial Stenosis.—Total bronchial stenosis is reported to cause constant atelectasis with venous stasis on the operated side. It has also been noted that subsequent tuberculous lesions were always of a lesser degree in the atelectatic lung, as compared with the lesions in the contralateral lung. Pathogenetic interpretations of this phenomenon have generally been based on the decrease of intrapulmonary oxygen and on a chronic circulatory stasis. The author would add the influence of the functional rest of the lung as another reason for the milder lesions caused in an atelectatic lung. On the basis of former personal researches that had demonstrated that partial stenosis of the upper respiratory tract aggravates tuberculous pulmonary lesions (perhaps because of exaggerated respiratory activity), while also creating a respiratory stasis, Maccone has made further investigations with partial stenosis of one main stem bronchus; the other main stem bronchus was left patent and served as control for observation of anatomical changes in the operated side. Rabbits of 2.5 to 3.0 kg. were used. After inducing a small pneumothorax the previous day, the right main stem bronchus was ligated so as not to entirely occlude its lumen. Of 8 healthy rabbits thus treated, 4 died within seven days and the other 4 died in 10 to 18 days. In all of the rabbits the left lung was found to be normal macroscopically and histologically; but the right lung was atelectatic and had areas of intraälveolar oedema in the first 4 rabbits that died early, while there was acute emphysema in the other 4 rabbits that died later. To study the influence of partial bronchial stenosis on the course of tuberculous lesions in an infected animal, several rabbits were inoculated with a large dose of a known strain of bovine tubercle bacilli either twenty days before the ligation of the bronchus, at the same time, or several days after the ligation. Practically all these rabbits developed miliary or caseous lesions in both lungs, but their progression was more rapid and more severe in the right than in the left lung. The origin of the circulatory changes and of the grave emphysema in the healthy rabbits seems to be in the increase in the intrapulmonary elastic tension with subsequent increase in the negative intrapleural pressure, that cause breaks and lacerations of alveoli and septa. When tuberculous infection was added to the partial stenosis of the main bronchus, it is presumable that continuance of respiratory function, under conditions of increased pulmonary tension, constituted a harmful factor, and favored the evolution of specific processes in the handicapped lung.—*Alterazioni anatomiche successive a stenosi perziale di un grosso bronco in conigli sani e tubercolosi, V. Maccone, Ann. d. Ist. Carlo Forlanini, March–April, 1940, 4: 183.*—(*S. L.*)

Partial Stenosis of Trachea.—Variations of intrapulmonary elastic tension cannot be considered traumatic to the lung when a normal condition of patent bronchi and alveoli exists. But when patency of the bronchial tree is altered by reason of certain conditions, such as bronchitis, mucosal hyperplasia, tumors, etc., then the physiopathological and anatomical balance is more or less disturbed. A preliminary study of the effects of stenosis of the nasal passages failed to give constant results. This study was therefore made. The lumen of the trachea of normal rabbits was restricted with temporary silk ligatures. This procedure, though well tolerated by the animals, was followed by a marked increase in the frequency and depth of the respiratory function; the inspiratory thoracic expansion was decidedly restricted, and inspiratory and expiratory wheezing was audible. Intrapleural negative pressure was at higher levels than usually found in normal rabbits. Most of the animals with the tracheal ligature died within two weeks; some died in a few days. Several rabbits were sacrificed early by bleeding, in order to serve as controls to those that died naturally. In all of the animals macroscopical examination showed bilateral pulmonary congestion; scattered areas of superficial or parenchymal hyperaemia were frequently seen, usually in the upper lobes, with areas of atelectasis or emphysema. These lesions were less visible macroscopically in those animals which survived longest. In the animals that died early or that were sacrificed by bleeding a few days after the ligature, there was seen a constant and very marked turgescence of the

pulmonary veins and capillaries. Recent parenchymal haemorrhages, mostly peripheral or subpleural, were frequent. Several rabbits were found to have a marked alveolar or bronchial oedema. Little venous stasis or intraälveolar oedema and few haemorrhagic lesions were found in the animals that died later; bronchioles and alveoli were dilated and areas of initial atelectasis were seen. The conclusion is that the immediate result of tracheal stenosis is a marked circulatory stasis of short duration, with subsequent return to normal, followed by phenomena of mainly mechanical nature. The same experiments were carried out on rabbits given a constant dose of a known strain of tubercle bacilli (H 37) intravenously. The same massive circulatory changes, consisting of capillary stasis, oedema and haemorrhage, were noted. At first these changes were diffused through the whole parenchyma; later they localized at the periphery of the miliary foci, soon after their appearance. The specific lesions at first appeared to have a tendency to slower evolution than in animals similarly inoculated, but without tracheal stenosis; later, however, there was noted a tendency to the spread and confluence of the tuberculous lesions, with formation of giant cavities. It appears, therefore, that the abnormal increase of intrapulmonary elastic tension, caused by the partial stenosis of the trachea, acts predominantly on those areas of infiltrated parenchyma and determines their further destruction.—*Alterazoni anatomiche successive a stenosi parziale della trachea in conigli sani e tubercolosis, V. Maccone, Ann. d. Ist. Carlo Forlanini, November–December, 1939, 3: 885.*—(*S. L.*)

Effect of Amyl Nitrite on Bronchial Tree.—An attempt was made to demonstrate the effect of a nitrite on bronchial muscle in dogs and in man. In dogs, anaesthetized with intravenous nembutal, no dilatation of the bronchi was obtained, although constriction had been produced by pilocarpine. In these experiments the effect of the anaesthetic must be considered as it produces some relaxation of the bronchial muscles and would obviously diminish the degree of relaxation obtainable by inhalation of amyl nitrite. In most of the experiments in man, dilatation of the bronchi was obtained. Younger patients showed greater dilatation and the smaller bronchioles dilated more than the large bronchi. It is suggested that the drug may be of use in bronchostenosis and atelectasis.—*Observation on the Effect of Amyl Nitrite on the Bronchial Tree, W. F. Nicholson, J. Thoracic Surg., December, 1939, 9: 194.*—(*L. F. B.*)

Bronchial Plugs in Lobectomy.—A method is described in which silver plugs are used to close the bronchi in dogs. The silver plug consists of a hollow cylinder open at one end, with a transverse rod at the open end to facilitate removal, and a circumventing groove near the closed end to prevent the ligature from slipping. After a ligature was placed about the bronchus, the plug was inserted into the bronchus through a slit distal to the tie, and adjusted so that the groove lay at the site of the ligature. This method yielded uniformly good results when two lobes were removed. It is believed that the use of plugs eliminates to a great extent the lateral tension of the cartilaginous rings as well as the pressure of the ligature. Subpleural, subserosal and subadventitial insertion of the ligature aids in maintaining the blood supply to the tissues of the lobectomy stump.—*Experimental Lobectomy Using Bronchial Plugs, S. R. Rosenthal, E. H. Lambert, W. Van Hazel & P. H. Holinger, J. Thoracic Surg., August, 1939, 8: 668.*—(*L. F. B.*)

Intrabronchial Pressures and Mediastinal Emphysema.—In giving intratracheal insufflation anaesthetics, there are many factors which enter into smooth operative and postoperative course. Although this type of anaesthesia has made tremendous advances, too many unexplained fatalities occur. After the death of several animals following chest operations under intratracheal anaesthesia, studies were made of ingoing pressures, intratracheal pressures, changes in blood pressures and in respiratory movements. An intratracheal catheter was employed, delivering a continuous stream of air and ether to the lower end of the trachea. Intrabronchial pressure was regulated by the amount of resistance to air escaping from the

lungs through a tube connected with a tight fitting face mask. Maximum intrabronchial pressures were varied from 16 to 110 mm. of mercury. The accompanying fall in blood pressure varied from 8 points, with a 6 mm. rise in intrabronchial pressure to 98 points with a 100 mm. rise in intrabronchial pressure. Pressures of 24 mm. of mercury or over were routinely accompanied by the development of emphysema, in dogs, usually along the great vessels at the hilum of the lung. Once induced, emphysema was continued at a pressure lower than that required to start it. In cats, pressures of 16 to 20 mm. of mercury resulted in emphysema. It is believed by Macklin that air in finely subdivided form breaks through from the alveoli abutting upon the perivascular sheaths into the perivascular tissue. He has not pointed out that after the chest is opened and increased intrabronchial pressure applied, emphysema occurs more easily, as there is then greater stretching of the perivascular tissue with less pressure because of removal of the restraining chest wall. Increased intrabronchial pressure either by intratracheal or mask anaesthesia technique may produce deleterious effects by overdistention and laceration of intrapulmonary tissue with subsequent development of emphysema and pneumothorax. Intrabronchial pressure depends chiefly on the patency of the outlet. Extremely high intrabronchial pressures are necessary to cause emphysema about the neck and face or to cause right heart failure in dogs. Pneumothorax may easily occur following mediastinal emphysema.—*Differential Intrabronchial Pressures and Mediastinal Emphysema, R. J. Marcotte, F. J. Phillips, M. W. Adams & H. Livingstone, J. Thoracic Surg., February, 1940, 9: 346.*—(*L. F. B.*)

Tuberculous Synovitis from Avian Bacilli.—Ten yearling bulls were injected intravenously with strains of avian tubercle bacilli recovered from swine. The dose was 5 mg. of culture, moist weight, suspended in 5 cc. of saline. Six of the 10 animals died of tuberculous pneumonia thirty-one to fifty-four days following injection. Eight months after inoculation, 2 of the remaining 4 animals developed swellings in various joints of the extremities. Avian tubercle bacilli were cultured from fluid removed from the joints. One animal died two years after inoculation and the other was sacrificed, in a weakened condition, almost three years after inoculation. Joint enlargement was due to thickening of the synovial membrane and capsule. There was no evidence of ankylosis or bone destruction. There was no evidence of organic tuberculosis in these 2 animals. The 2 remaining animals appeared to be in good condition throughout the course of the experiment. Both were sacrificed and on postmortem examination only one showed any abnormality. This animal had been castrated by pinching the spermatic cord. Organisms culturally like avian tubercle bacilli were cultured from the thin watery seminal fluid. A well encapsulated abscess was found in the omental fat below the rectum. Organisms, culturally like avian tubercle bacilli, were cultured from this abscess.—*Tuberculous Synovitis in Bovines Resulting from the Intravenous Injection of Avian Tubercle Bacilli, A. B. Crawford & A. H. Frank, J. Am. Vet. M. A., April, 1940, 96: 459.*—(*L. F. B.*)

Testosterone in Tuberculosis.—The mortality rate among individuals infected with tuberculosis shows striking differences at different periods of life. Following the very high case fatality rate of infancy there comes a period from five years to puberty when the low death rate is truly remarkable. This period of grace is followed in turn by a mounting rate of mortality in adolescent years and never again does it return to the low level of childhood. That this accentuation in the gravity of the disease is synchronous with the development of sexual maturity has long been noted. Children, before the age of puberty, are not known to excrete estrogenic hormones in their urine. Some androgenic activity, however, may be present early and the observations of Oesting and Webster indicate that there is a definite and significant rise in this factor at about the sixth year and a steady rise thereafter. An attempt was made to study the effect of androgen (testosterone propionate, Ciba) on infant guinea pigs infected with tuberculosis. Male guinea pig nurslings, three to

five days old were selected. Every other animal received a subcutaneous implantation of two pellets of the androgen in the skin of the back. Three days later, every young animal was infected with a small dose of human tubercle bacilli. The mothers were removed from the cages when the average age of the young was twenty-eight days. Four weeks after infection each animal was skin tested with 10 mg. of OT. On the forty-second day after infection all the animals were killed and carefully examined. Each pellet of testosterone propionate was recovered and weighed. None of the animals died during the course of the experiment and none showed signs of severe illness. There was no significant difference in the extent of the disease in the two groups. Both showed a similar degree of sensitivity to tuberculin. The average absorption of the drug was 7.2 mg. per guinea pig. That the drug was potent and effective was indicated by the fact that the testes of the treated group were invariably much smaller than those of the control animals and showed a retardation of development of the tubules.—*The Effect of Testosterone Propionate on the Development of Tuberculosis in the Immature Male Guinea Pig, W. H. Carnes & G. R. Biskind, Bull. Johns Hopkins Hosp., May, 1940, 66: 297.*—(*J. S. W.*)

Lung Changes in Cardiozol Convulsions.—Seventeen dogs were given 20 to 30 mg. per kilo of cardiozol intravenously. Two died after the convulsions with massive pulmonary oedema. Fourteen survived but showed definite disturbances: respiratory movements were forced and frequent, and the carotid blood showed a marked oxygen deficit. There was also marked cyanosis which could be alleviated by administration of oxygen. When the surviving animals were sacrificed, marked changes were found in the lungs. These consisted chiefly of hyperaemia, oedema and actual blood in the alveoli. There was also marked widening of the capillaries. Oedema was present mainly in the lower lobes. The pulmonary changes varied, in large degree, with the intensity of oxygen deficit. The oxygen saturation in these animals ranged from 64 per cent to 93 per cent. Some of these animals were able to get along when apparently only one quarter of the total lung area was functioning. In these dogs the convulsions lasted from three to ten minutes and manifested constantly a tetanic phase with opisthotonus. The pulmonary oedema came on within a few minutes after onset of the convulsions. Similar results were obtained in 18 rats and 10 guinea pigs injected with cardiozol. Several factors must be considered in attempting to account for these pulmonary changes. During the convulsions bradycardia is a constant finding. This appears to be a result of the marked oxygen deficit. Previous X-ray studies have shown marked cardiac dilatation during the convulsive phase, indicative of cardiac failure. There is also marked shunting of the blood from the greater to the lesser circulation with consequent overloading of the latter. This is due to the generalized muscular contractions which drive the blood into the pulmonary circulation. Finally, as the result of central nervous system stimulation, there is sympathetic stimulation of the pulmonary vessels resulting in capillary widening, stasis and congestion.—*Lungenveränderungen im Cardiazolkrampf, A. Jarisch & H. Thoma, Klin. Wchnschr., January 27, 1940, 19: 76.*—(*H. R. N.*)

Spread of Substances in the Skin.—The spread of India ink and of haemoglobin in the skin of rabbits, three to eighteen months of age, is a sex limited character, the females spreading both to a greater degree. The spreading power was greater in both males and females of tuberculosis-susceptible families than in those of resistant families, and corresponded to the spread of tuberculosis in the tissues.—*Relative Spread of Particulate and Diffusible Substances in the Skin of Male and Female Rabbits, M. B. Lurie & P. Zappasodi, Proc. Soc. Exper. Biol. & Med., December, 1939, 42: 741.*—(*F. B. S.*)

Antisyphilitic Treatment in Syphilitic Rabbits with Tuberculosis.—Arsphenamine was injected into rabbits infected with *Tr. pallidum*, and three weeks later they were infected intracutaneously with bovine type tubercle bacilli. Histological study of the sites of inoc-

ulation removed at various intervals showed that the development of the local lesions was identical with the course in untreated syphilitic rabbits similarly inoculated with tubercle bacilli.—*Effect of Antisyphilitic Treatment on Histopathology of Local Tuberculous Lesions in Syphilitic Rabbits, J. D. Aronson & D. R. Meranze, Proc. Soc. Exper. Biol. & Med., January, 1940, 43: 83.*—(*F. B. S.*)

Action of Dust and Dead Tubercle Bacilli.—Sandstone dust, slate quarry dust, quartz and anthracite dust, when injected intratracheally in rabbits together with dead tubercle bacilli, all produced much larger and more cellular lesions than the various dusts without the bacilli. The substitution of 40 mg. of tuberculin for the dead tubercle bacilli had no effect on the augmentation of the lesions. The amplified lesions appeared due to the combined action of dust and tubercle bacilli.—*The Augmentation of Actions of Anthracite and Other Dusts by Dead Tubercle Bacilli, S. L. Cummins, Brit. J. Exper. Path., February, 1940, 21: 64.*—(*H. J. H.*)

Sedimentation Test.—Day separates the process of erythrocyte sedimentation into phases and attempts to evaluate the influence of various factors on each phase. There is the period of acceleration, from the zero mark to the period of maximum velocity where the curve is steepest, followed by the period of packing where it slows down to a horizontal level. In pulmonary tuberculosis the most rapid increase in sedimentation rate occurs at the onset of acute pleural effusion and the most rapid decrease when such effusion is either reabsorbed or ceases to cause constitutional symptoms. If fresh pleural fluid is added to blood plasma its agglutinating properties are identical but more marked. Technique is important in performing this test and the best technique is that which registers the subtlest range of variations. Columns of less than 2 mm. diameter introduce hydrodynamic factors which distort the results. The higher the column the longer the phase of maximum velocity and the more constant the one hour readings. In clinical work the 200 mm. Westergren tube seems most satisfactory but it requires 1.6 cc. of blood. For an anticoagulant 3.8 per cent sodium citrate in physiological saline is best, oxalate giving more erratic results. This of course involves a dilution of the blood, but such dilution does not affect the results until the cell volume is less than 14 per cent of the whole blood, e.g. in pernicious anaemia, where some plasma must be pipetted off to maintain corpuscular rate. The nonspecificity of blood sedimentation rate is emphasized. Although sedimentation seems to be a product of tissue destruction there is no constant connection between the sedimentation rate and the phenomena of toxaemia. Insufficient studies have been made on its behavior in the course of the exanthemata or acute trauma. In any given case serial or comparative readings are important.—*The Behavior of Sedimenting Blood, G. Day, Tubercle, May, 1939, 20: 364.*—(*A. P.*)

Conglobation Reaction in Tuberculosis.—The Haag conglobation reaction is specific for tuberculosis. Its results are parallel to those of the complement fixation reaction, but are more often positive in patients with tuberculosis, as well as in patients without tuberculosis. To avoid the nonspecific reaction, the author improved the method. He used not only the undiluted serum, but also a serum diluted 1:4 and a serum previously absorbed with the Mueller conglobation reagent, and the antigen of Witebsky-Klingenstein-Kuhn. In 195 cases of far advanced pulmonary tuberculosis 66.2 per cent showed a positive conglobation reaction with the undiluted serum, 56.4 per cent with the diluted serum and 50.8 per cent with the absorbed serum. The exudative cases were more often positive than the productive ones. Of the patients with positive sputum 77.5 per cent gave a positive reaction with the undiluted serum, 68.9 per cent with the diluted serum and 64.2 per cent with the absorbed serum. The respective figures for cases with negative sputum were 27.3 per cent, 13.6 per cent and 4.5 per cent. In patients with early tuberculosis there was a positive reaction with the undiluted serum in 43.2 per cent, with the diluted serum in 30.9 per cent and with the absorbed serum in 30.9 per cent. The respec-

tive figures for primary tuberculosis were 21.5 per cent, 12.6 per cent and 11 per cent, for pleuroperitonitis 46.8 per cent, 40.3 per cent and 33.9 per cent, for exudative pleuritis 38.8 per cent, 22.4 per cent and 18.4 per cent. Patients who always reacted negatively were numerous among those who had a recent history or who showed slight symptoms and among those who were seriously ill or died. Patients who always reacted positively were often among those who had a far advanced disease or a history of long duration. In 855 patients without tuberculosis the conglobation reaction was positive with the undiluted serum in 17.8 per cent, with the diluted in 9.2 per cent and with the absorbed in 3.6 per cent. In 2121 healthy subjects the respective figures were 10.8 per cent, 3.9 per cent and 2 per cent, without any significant difference between the sexes. The conglobation reaction turned negative in 8 cases before or after the complete disappearance of tubercle bacilli in sputum, in 3 cases within 3 months after the disappearance of tubercle bacilli and in 4 cases when the sputum turned negative on direct smear. No parallelism existed between the conglobation reaction and the tuberculin reaction. Among 90 patients with pulmonary tuberculosis 60 per cent showed a complete parallelism between the results of the conglobation reaction and those of the complement fixation reaction. Antigen activated by picric acid gives the highest number of positive results in tuberculous as well as in nontuberculous subjects; antigen activated with resorcin gives a smaller number of positive results. The conglobation reaction with absorbed serum is usually also negative in cases with a positive Wassermann reaction; it can, therefore, be used for the differential diagnosis of tuberculosis complicated by lues.—*Ueber die Ballungsreaktion bei der Tuberkulose, Y. Kaziwara, Tohoku J. Exper. Med., July 5, 1940, 38: 443.*—(*G. C. L.*)

Takata Reaction in Tuberculosis.—Three hundred and five Takata reactions, in the modification by Öfelein, were performed in the serum of 195 patients with tuberculosis and in 20 normal subjects. This method seemed to be of help in ascertaining the activity of a pulmonary process. In some cases it was superior to the sedimentation reaction of erythrocytes.—*Die Takata-Reaktion in der Modifikation nach Öfelein als Aktivitätsreaktion bei Lungentuberkulose, G. Koch, Ztschr. f. Tuberk., October, 1939, 83: 200.*—(*G. C. L.*)

Carbonic Anhydrase in Tuberculosis.—This catalytic agent, of enzymic nature, was isolated by Meldrum and Roughta (1932 and 1933) and the name suggested by Eggleston. Its presence is vital since it enables the blood to quickly eliminate carbon dioxide while passing through the lung. The method employed for measuring its activity was that devised by Brinkman, Margaria and Roughton, of a simple manometric type in which the rate of evolution of carbon dioxide from a mixture of bicarbonate and phosphate buffer of pH 6.8 is the measure of enzymic activity. The carbonic anhydrase of 17 normal rabbits was found to vary between 1.18E and 2.26E with an average of 1.56E per cc. whole blood and from 2.92E to 6.4E with an average of 4.2E per cc. of red corpuscles. In rabbits infected with tuberculosis, while the average value remained unchanged much lower values were observed in individual rabbits (e.g. reduced to one-half or one-third). This marked fall could not be ascribed to reduction in the red cells but might be attributed to a toxin, not necessarily specific. Similar low findings have been observed in the blood of human subjects suffering from prolonged pyrexia.—*The Effect of Tuberculous Infection on Carbonic Anhydrase of Rabbits Blood, C. Shiskin, Tubercle, February, 1939, 20: 227.*—(*A. P.*)

Levinson and Tryptophan Tests in Tuberculous Meningitis.—In 18 cases of tuberculous meningitis (as proven by the bacteriological findings of tubercle bacilli in the spinal fluid and positive autopsy findings) 18 had positive Levinson tests; 16 showed positive tryptophan-A tests; 12 showed positive tryptophan-B tests; 2 showed negative tryptophan-A and B tests. In 8 cases of nontuberculous meningitis with clear spinal fluids, in which the diagnosis was either lethargic encephalitis, brain abscess, choriomeningitis or polyencephalitis, there were 8 positive tryptophan-A

tests and 3 positive tryptophan-B tests. All 8 had negative Levinson tests. Seven bloody and 9 purulent spinal fluids all gave positive Levinson and tryptophan tests.—*Comparative Value of Levinson and Tryptophan Tests in the Diagnosis of Tuberculous Meningitis, M. Gleich & Roslyn Weintraub, Arch. Pediat., November, 1939, 56: 749.*—(*M. B.*)

Vitamin A.—The vitamin-A content of human livers was determined photometrically in 50 patients in whom tuberculosis was the cause of death. In these patients the vitamin-A content of the diet averaged from 5000 to 8000 U.S.P. units per day. All patients were fed the general hospital diet but 6 were given a supplemental dosage of vitamin A. The average vitamin-A content of the livers was 342 U.S.P. units per gram and this was essentially the same regardless of the duration of the disease. However, in the presence of a febrile course in excess of 100° F., the vitamin-A content of the liver was about 50 per cent less than in those patients who were relatively afebrile. In patients with tuberculous enteritis the vitamin-A content was considerably lower than in patients not so affected. The average liver content compares favorably with that reported for healthy persons and it is apparent that the high vitamin diet of the tuberculosis hospital furnishes sufficient vitamin A for storage. In individuals with tuberculous enteritis extra quantities of vitamin A should be provided in the diet.—*Vitamin A Content of the Human Liver in Tuberculosis, P. D. Crimm & D. M. Short, Ann. Int. Med., July, 1939, 13: 61.*—(*A. A. E.*)

Pulmonary Function.—With the introduction of newer techniques in the study of respiratory function, there has been increasing realization of the importance of such studies in pulmonary tuberculosis. Respiratory studies on cases of pulmonary tuberculosis, both on bed-rest and under collapse treatment, have shown definite evidence of oxygen deficit and increased respiratory work where these were not previously suspected. Rest of the lung, as far as possible, is one of the prime considerations in the treatment of pulmonary tuberculosis, yet in many cases functional studies on patients under treatment will show increased respiratory work. Moreover, the accompanying arterial oxygen deficit over a prolonged period has an injurious general effect on the body and carries with it an unfavorable prognosis. These unfavorable factors both in collapsed and uncollapsed lungs can often be overcome by having the patient breathe oxygen in concentrations of from 25 to 30 per cent. Oxygen therapy in this manner can be carried out over long periods with good results. In pneumothorax therapy, oxygen deficit can sometimes be relieved by varying the refills. For example, larger refills with increased collapse of the lung will often accomplish this result. These factors can only be gauged by frequent and careful studies of respiratory function. Further studies in this field are needed but enough has been done to demonstrate the great importance of these methods in lung disease. Illustrative case histories are presented.—*Einige Bemerkungen zur Behandlung der Lungentuberkulose, G. Petzold & G. Zaeper, Klin. Wchnschr., September 30, 1939, 18: 1289.*—(*H. R. N.*)

Respiratory Defense Mechanism.—Because of certain observations in persons with lung abscesses a study was undertaken to determine any changes in the respiratory defense mechanism and whether any relationship could be demonstrated between this mechanism and pulmonary diseases. The pharyngeal, laryngeal and tracheobronchial reflexes were tested in several groups of patients including those with lung abscesses, bronchiectasis, chronic lung diseases and persons apparently free of pulmonary disease. The pharyngeal and laryngeal reflexes were tested in all, and the tracheobronchial in a limited number. The general neurosensitivity of each was recorded. A detailed history was obtained with especial attention to mouth infections, the use of alcohol and sleeping habits. Examinations were also made on adults during sleep, adults asleep under the influence of alcohol or sedatives, and infants and children during sleep. In the latter groups 5 cc. of lipiodol were instilled into the nose or mouth of the sleeping individual and X-ray films taken after two to five hours. One in 4 persons was found to

have a depressed pharyngeal reflex and 1 in 6 had a depressed laryngeal reflex. In the abscess group one in 2 revealed depressed reflexes, while one in 3 alcoholics showed this. The tracheobronchial reflex was the least effective. In those with chronic pulmonary disease no alterations were noted in the respiratory defense mechanisms and the findings were similar to those in the control group. In the entire control group of 333 tested for pharyngeal and laryngeal reflexes, 228 ran parallel. The laryngeal reflex was more sensitive than the pharyngeal in the remaining 105. Considering the entire series, the degree of reaction of both reflexes was the same in 2 out of 3 cases, and the laryngeal reflex was the most sensitive in one out of 3 cases. Cough was most frequently associated with the laryngeal reflex. The pharyngeal and laryngeal reflexes ran parallel to the general neurosensitivity in 457 of the 620 individuals analyzed. Thus in 3 out of 4 cases the general neurosensitivity was an index of the activity of the respiratory defense mechanism. In the 100 cases of so-called idiopathic lung abscess studied an aetiological basis could be assigned in about 85 per cent. The background consisted of some focus of infection in the upper respiratory tract, especially pyorrhoëa, and some break in the respiratory defense mechanism, especially alcohol, and an inherent state of depressed reflexes. Reviewing 50 cases of bronchiectasis, sinusitis with a noticeable postnasal drip was found in 14, 7 of whom showed a natural depression of the respiratory defense mechanism. Of those observed under altered conditions, 4 in 25 aspirated material (lipiodol) during ordinary sleep, 14 of 25 aspirated material when asleep under alcohol and 4 in 10 aspirated material when asleep under the influence of sedatives. Oil was noted in the lung of only one child tested during sleep and this child was debilitated. The observations made during the testing of the sleeping persons suggest that swallowing, spitting and drooling also serve as a means of protection. Of these, the outstanding protective mechanism in most cases was swallowing. After lipiodal injection, coughing and retrograde peristalsis were most active during the first few minutes. Following this short period a dormant phase occurred, the lipiodol remaining in the lungs for as long as several days. Thus the study shows that the laryngeal reflex is the real "watch-dog" of the lungs. The pharyngeal reflex is next in importance and the tracheobronchial system is the least effective. Once fluid passes the larynx the possibility of retention and subsequent damage is increased and, while there are other modes of protection, undoubtedly some foreign material remains in a few cases and results in a definite pathological condition. Cough is an important defense mechanism but is not present at all times and is particularly absent when the foreign material is not a coarse object or produces no chemical irritation. Therefore, it is important to avoid anything that will depress all the reflexes. Unfortunately, in a few persons an inherent lowered sensitivity occurs which may be sufficiently active during conscious periods but affords inadequate protection during sleep or other altered conditions. In the past both alcohol and sedatives have been employed in upper respiratory infections, sometimes without moderation; this undoubtedly is a mistake. In the abscess group it is to be noted that over 50 per cent had inherently depressed reflexes and alcohol predominated among the factors tending to inhibit the defense mechanism. However, in considering histories, fainting spells, epilepsy, submersion and precomatose states are of importance. A break in the normal mechanism is also noted in postoperative abscess and the results of this study suggest that aspiration is the chief aetiological factor in a majority of such cases. Pyorrhoea is the most common form of upper respiratory infection, although sinusitis, tonsillitis, and infected teeth cannot be forgotten. Diseased mouths were found in 84 per cent of idiopathic abscesses studied by Stern and numerous investigators have demonstrated the facility with which material from the mouth and pharynx is aspirated. The author reiterates that the study demonstrates an important triad, namely alcohol, an inherently depressed respiratory mechanism and pyorrhoea and that the average lung abscess case may truly be described as a "middle aged male, pyorhoetic, with a tendency to bouts of alcohol." In the past the cause of lung abscess has been difficult to

determine in many cases. However, if one bears in mind and searches for two factors, a focus of infection in the upper respiratory tract and a transient or permanent defect in the respiratory defense mechanism, the problem will easily be solved. A mechanism similar to that described in the production of lung abscess is also possible in other diseases. It probably plays an important rôle in a large percentage of bronchiectasis and may even play a rôle in the development of pneumonia, bronchopneumonia and suppurative pneumonitis. This seems more probable when the bacteria frequently found in persons with upper respiratory infections are considered. Certain prophylactic measures are indicated. These include the treatment of all respiratory foci, the avoidance of all factors tending to diminish the respiratory defense mechanism and the clearing completely of upper respiratory infections in persons with inherently lowered reflexes as quickly as possible.—*The Respiratory Defense Mechanism: Its Relationship to Pulmonary Diseases, I. J. Applebaum, Am. J. M. Sc., September, 1939, 198: 356.*—(*G. F. M.*)

Bronchospirometry.—The author describes a specially constructed instrument for simultaneously measuring and recording the functional capacity of each lung separately. The findings in 7 cases are presented. The catheter is made of rubber and has a natural curve to facilitate its entry into the left main bronchus. A fine steel spring is embedded in the wall and imparts a desirable semirigidity to the instrument and makes it noncollapsible. A dividing septum separates the air passage from each lung. The wall contains a fine channel through which two balloons may be inflated to seal off the left main bronchus and the trachea, thus confining each lung to a separate spirometer. The catheters are graded in size. "Metabolors" were used in this study.—*A Catheter for Bronchospirometry, P. W. Gebauer, J. Thoracic Surg., August, 1939, 8: 674.*—(*L. F. B.*)

Respiratory Rhythmicity.—Because of the difference in concept of the origin of respiratory rhythm, a study was made of the brain stem mechanism for the site of the respiratory centre, the pathways of connection with the respiratory centre and the significance of the changes in the respiratory rate of panting and pain polypnoea. Lesions were made in cats and the respirations were recorded with and without cold blocking of the vagi. It was found that the rhythmicity of respiration is not an inherent process but results from the activity of two bilateral mechanisms, a brain stem pneumotaxic centre and a vagal reflex system sensitive to lung stretch. These two mechanisms are similar to each other and mutually replaceable. A fraction of one of these two systems, active on one side only, is sufficient to impart rhythmicity to respiration. With both systems bilaterally and completely eliminated, a maintained tonic respiration (apneusis) results. The brain stem pneumotaxic centre has been localized to the tegmentum of the pons. The red nuclei and the inferior colliculi are of no functional significance in imparting rhythm to respiration. The pathways connecting the pneumotaxic centre with the medullary respiratory centre are located ventrally and far laterally in the pons and upper medulla, ventral and slightly medial to the descending root of the trigeminal nerve, so that in man these pathways, if similar, would probably be vulnerable in thrombosis of the posterior inferior cerebellar artery or in trigeminal trachotomy. Although the posterior root proprioceptive and the cutaneous sensations modify the respiratory rhythm they cannot substitute for the above mechanisms. To account for the action of the pneumotaxic centre it is postulated that the act of inspiration sets up impulses in the ascending pathways to the pneumotaxic centre, which through a closed neuron arc leads to inspiratory inhibition in a manner analagous to the inhibition caused by the reflex stimulation of the vagal afferents. Decorticate and polypnoeic panting is probably mediated through the pneumotaxic center and its descending pathways by facilitation from some higher mechanism released from cortical control. Reflex pain polypnoea may be produced only in the presence of some functional rhythmic drive. When this drive is eliminated (apneusis), sensory stimulation leads only to slight de-

crease or increase of the tonic inspiration. The authors are unable to answer with any certainty whether or not the respiratory centre has any spontaneous activity. However, they feel that if the activity is spontaneous, such activity is confined to the inspiratory center, but the nature and the origin of its initial discharge still remains unknown. Spontaneous rhythmicity is not a property of the medullary respiratory centre.—*The Origin of Respiratory Rhythmicity, R. F. Pitts, H. W. Magoun & S. W. Ranson, Am. J. Physiol., November, 1939, 127: 654.*—(*M. A. B.*)

Pneumothorax Gases.—Since the use of artificial pneumothorax in the treatment of pulmonary tuberculosis, many workers have been interested in the composition of air present in the pleural cavity. In a healthy pleural cavity, equilibrium is established in the course of several days after the introduction of any gas and the mixture again has the same composition as before, namely 2 to 4 per cent oxygen and 6 to 8 per cent carbon dioxide. In pulmonary tuberculosis the composition of intrapleural air is altered by variations in the degree of collapse, histologic changes in the pleura, the presence or absence of fluid and bronchopleural fistulae. In 1932 Coryllos published a report of analyses of air in artificial pneumothorax and found a high degree of correlation between the composition of intrapleural air and the type of fluid, if any, in the pleural cavity. He also found a high percentage of oxygen and low carbon dioxide tension in bronchopleural fistula. This study was undertaken in an attempt to confirm Coryllos' findings and, if possible, apply them in the management of artificial pneumothorax. Seventy-four analyses were made on thirty-five patients and, whenever possible, findings were checked postmortem. An attempt was made to classify the results according to the fluid present as Coryllos had done, but it was found that the composition of intrapleural air, especially in cases of long standing pneumothorax, was so modified by other factors as to limit the usefulness of such a classification. Oxygen values especially were difficult to interpret in terms of any single factor. There was a tendency for them to vary inversely with carbon dioxide values. A fair degree of correlation was found between carbon dioxide tension and the purulency of the fluid except in cases of intermittent formation and reabsorption. Oxygen values, as demonstrated by Coryllos, were found useful in the diagnosis of small fistulae periodically closed by fluid. The authors feel that serial analyses give more reliable data and should always be performed when possible.—*The Composition of Intrapleural Air in Artificial Pneumothorax, A. T. Miller & J. M. Jones, Am. J. M. Sc., April, 1940, 199: 564.*—(*G. F. M.*)

Pneumothorax Gases.—Forty-three patients with pneumothorax were studied by means of analysis of the pneumothorax air and estimations of the amount of exudate. Thirty-five of these patients had pleuritis with effusion. Of these 9 had a simple transient pleuritis with effusion, 7 had mild tuberculous pleurisy in which the fluid was serofibrinous or seropurulent, 11 had chronic tuberculous pleurisy with persistent purulent fluid which usually contained small numbers of tubercle bacilli, 4 had acute tuberculous pleuritis with effusion and marked febrile reactions and 4 patients had mixed tuberculous empyema. In a dry pneumothorax there is a progressive decrease in the average daily absorption rate of the pneumothorax air; this decrease is more marked in the initial months and becomes gradually less. The effect of a transient pleuritis and effusion upon the absorption rate of pneumothorax air is variable. A mild tuberculous pleuritis and effusion causes marked acceleration of the absorption rate of pneumothorax air in the early stages and then an absorption rate that approaches that of a dry pneumothorax. With the more severe forms of pleuritis and effusion there is considerable diminution in the absorption rate of air. The amount of this decrease varies directly with the intensity of the pleuritis and after the acute stage has passed there is a progressive and gradual decrease in the absorption rate. The diffusion rate of carbon dioxide is not significantly affected by the duration of the pneumothorax or by a complicating pleuritis and effusion. However, the diffusion rate of oxygen decreases with the increasing

duration of the pneumothorax. Pleuritis and effusions cause a more marked decrease in the diffusion rate of oxygen with a variation in this decrease depending upon the duration of the pneumothorax, the duration and character of the exudate and the severity of the pleuritis. In the absence of an effusion, the composition of the pneumothorax gases after an initial brief period of marked change, is stable as long as a given collapse of a lung is maintained. The pH of the pneumothorax exudate varies with the severity of the pleuritis and ranges from about 7.32 in serous exudates to 6.47 in a mixed tuberculous infection. The carbon dioxide content shows the same changes and with a decrease in the alkalinity and increase in the acidity of the exudate there occurs an increase in the carbon dioxide content of the pneumothorax air. Anatomical, roentgenographic and thoracoscopic examinations show that a gradual thickening of the pleura takes place during the course of an artificial pneumothorax. A passive hyperaemia of the pleural vessels and increased metabolism of the inflammatory tissue account for the initial increase in carbon dioxide and decrease in oxygen in pneumothorax pleuritis. Since vascular changes precede the formation of the effusion, the finding of quantitative changes in the pneumothorax gas tensions in a previously dry pneumothorax usually means an oncoming effusion. Since the absorption rate of pneumothorax air depends chiefly upon the diffusion of nitrogen, a lowering of the nitrogen tension of the blood by oxygen inhalation or of the pneumothorax air by replacement with a more readily diffusible gas, will cause an increase in the absorption of pneumothorax air. On the basis of quantitative changes in the pneumothorax gases, the diagnosis of the form of pleuritis and effusion may be made. There is a parallel between the intensity of the pleuritis and the carbon dioxide tension so that in the presence of a simple serous effusion the carbon dioxide tension is lower than in more severe pleurisy. The cases with simple effusions have slight or no changes in pneumothorax gas tensions and these changes are much more apparent in individuals with more severe pleural infection; the greatest changes occur in the mixed tuberculous infections. Often the carbon dioxide and oxygen tensions are not completely restored to their original levels after the subsidence of a pleural infection. Thus the finding of a pneumothorax carbon dioxide volume of 7 to 9 per cent in a dry pneumothorax is usually indicative of a previous transient pleuritis and effusion. A chronic tuberculous pleuritis is similar in its earlier stages to the transient type, but the persistence of the exudate and its subsequent purulent transformation, together with the higher pneumothorax carbon dioxide tension, provide distinguishing features. Cases with a persistently high carbon dioxide tension of 12 to 13 per cent usually have small or valvular bronchopleural fistulae. The carbon dioxide tension in acute tuberculous pleuritis with a purulent exudate is about the maximum observed in a pure tuberculous infection. Those individuals with mixed tuberculous pleuritis may have an even higher carbon dioxide content and in some cases the oxygen tension may be zero. In pleuritis due to streptococcus or pneumococcus the inflammatory changes are considerably more marked than in the tuberculous types and this is reflected in the fact that the carbon dioxide content may be as high as 26 per cent with only 0.03 per cent oxygen. Putrid empyemata have a still higher carbon dioxide tension and often hydrogen, methane and hydrogen sulfide gases may be present. In comparison with blood all exudates are acid and the more acute the inflammation, the lower is the pH volume of the exudate.—*The Effect of Pneumothorax Pleuritis and Effusions upon the Behavior of Pneumothorax Gases, D. Matsuzawa, Quart. Bull. Sea View Hosp., October, 1939, 5: 40.*—(*A. A. E.*)

Movement of Diaphragm.—The mechanical theory of respiratory movements holds that in deepest inspiration the limits of expansion of the chest wall and descent of the diaphragm are reached. In a like manner, in deepest expiration the limits of contraction of the chest wall and ascent of the diaphragm are reached. The movements of the chest wall and diaphragm go together and it is felt that, at all times, these movements are dependent upon changes in lung volume. Other workers have shown that this purely mechanical ex-

planation is incorrect. The authors were able to corroborate these findings by roentgenkymographic studies of the respiratory movements of normal subjects. These studies showed that after deepest inspiration, without any change in lung volume, definite movements of the diaphragm can be observed when the abdominal wall is further sucked inwards. The diaphragm rises and is accompanied by further expansion of the chest, mainly in the region of the middle and lower ribs. This is a true paradoxical movement. In the same manner opposite movements of the chest and diaphragm are observed after deepest expiration when the abdominal wall is further protruded. These observations demonstrate that, at the end of deepest normal respiratory movements, both the chest wall and diaphragm are capable of further movement without changes in lung volume. In addition to mechanical factors, certain nervous influences must play a part in producing these changes.—*Grundsätzliches über die Begrenzung der Zwerchfellbewegungen, A. J. Anthony & M. Broglie, Klin. Wchnschr., August 19, 1939, 18: 1126.*—(*H. R. N.*)

Expired Water.—Based on a comprehensive review of the literature on this subject, a study is made on healthy subjects of varying age groups and on a group of patients with various types of pulmonary tuberculosis. Tables are presented indicating findings in detail. Healthy individuals eliminate water, varying in amount between 300 and 600 cc. daily, according to the age of the individual. This amount is highest in the third decade of life, lower in the fourth decade, and there is more elimination of water when breathing is deeper and less frequent. The amount of water eliminated by the pulmonary route is in direct relation to the amount of air exhaled. The amount of water eliminated by this route is generally higher in those suffering from pulmonary tuberculosis than in healthy individuals. It decreases, however, in quantity as exudative lesions become fibrosed, and it also decreases when any form of therapeutic collapse reduces the alveolar spaces, until finally the amount of water excreted becomes equal to, or even less than that of healthy subjects. The author concludes that the water eliminated by expiration is mainly from the alveolar spaces. This research confirms previous observations that the more perfect the pulmonary ventilation following a deep respiration, the more rapid and deep is the gaseous exchange.—*L'acqua espirata in soggetti sani ed in soggetti affetti da tubercolosi polmonare, A. Cimino, Riv. di pat. e clin. d. tuberc., September, 1939, 13: 642.*—(*S. L.*)

Intravenous Oxygen in Anoxaemia.—A study of the circulatory and respiratory responses to the intravenous administration of oxygen and their relation to anoxemia in dogs is presented. The average maintenance dose of oxygen was only about 2 to 3 cc. per kilogram of body weight. In the six dogs used there was a definite decrease in the arterial oxygen content as early as ten to fifteen seconds after the beginning of the injection showing that the oxygen administered intravenously cannot relieve a preëxisting anoxaemia, but can induce an anoxaemia. There was an abrupt increase of the respiratory rate of reflex origin, and section of the vagi prevented this increase. The arterial blood pressure fell when the rate of administering the oxygen was too rapid. The pressure in the right ventricle rose as soon as the oxygen was given and remained elevated until the gas was absorbed. This rise in the right ventricular pressure points to a disturbance of the pulmonary circulation, presumably a blocking of the blood channels by the gaseous emboli. The author found that increasing the inspired oxygen tension did not cause an increase in the arterial oxygen tension.—*The Respiratory and Circulatory Responses to Intravenous Oxygen and Their Relation to Anoxemia, M. Dick, Am. J. Physiol., September, 1939, 127: 228.*—(*M. A. B.*)

Ziehl-Neelsen Method.—Thanks to eponyms, names of scientists which otherwise would have been forgotten, are remembered. Eponyms are often arbitrarily chosen; this is also true for the Ziehl-Neelsen stain. In 1882, Robert Koch described a staining method with which he had discovered the tubercle bacillus. One month later, Paul Ehrlich published a much simpler and more reliable

method, which consisted of staining the preparation with a solution of methyl violet or fuchsin to which a saturated aqueous solution of anilin oil had been added. Koch admitted that Ehrlich's method was superior to his own and used it exclusively. Ziehl modified the method and introduced carbolic acid instead of anilin water. Neelsen recommended a fuchsin solution dissolved in 5 per cent carbolic acid to which a small amount of alcohol had been added. In contradistinction to Ehrlich, neither Ziehl nor Neelsen used a counterstain. The eponym, Ziehl-Neelsen, is therefore not justified for this method as it is only a slight modification of Ehrlich's method.—*Note on the Doubtful Propriety of the Eponym Ziehl-Neelsen for the Method of Staining Tubercle Bacilli, I. Snapper, Chinese M. J., December, 1939, **56:** 578.—(G. C. L.)*

Isolation of Tubercle Bacilli.—The Loewenstein technique for the isolation of tubercle bacilli as employed at the Vienna Pathological Institute is described in detail. The culture medium consists of a mixture of dipotassium phosphate, sodium citrate, magnesium sulphate and asparagin in distilled water. To this is added a mixture of human blood serum or hydrocoele fluid, glycerine, potato starch and malachite-green. The yolk and white of eggs are added and the mixture is shaken, tubed and sterilized for two hours at 100°C. in flowing steam, and resterilized for two successive days in the steam sterilizer. For the isolation of tubercle bacilli from the blood, 5 to 8 cc. of blood are drawn into a solution of "Liquoid." After shaking the blood, a watery solution of saponin and citric acid is added. The sediment obtained after centrifuging is washed twice with the saponin-citric acid solution, and is then acidified with several drops of sulphuric acid. The acidified sediment is washed twice with a buffer solution consisting of trisodium phosphate, tripotassium phosphate and sodium chlorate. The neutralized sediment is now planted on several tubes of the medium and smears are prepared from this sediment for staining by the Ziehl-Neelsen method. The isolation of tubercle bacilli from the various organs or tissues at post-mortem examination is made by first sterilizing the organ with a hot metal spatula or removing a piece of tissue measuring about 1 by 1.5 cm. by means of sterile instruments. Blood may be removed under sterile conditions from the heart. The tissue is ground in a sterile mortar and is acidified with 25 per cent sulphuric acid. If the organ is especially rich in blood, the citric acid-saponin solution is added. The treated tissue is centrifuged and the sediment treated with sulphuric acid for twenty to twenty-five minutes, when it is washed repeatedly with the buffer solution until it is no longer acid to litmus. The neutralized sediment is planted on the malachite-green medium. For the isolation of tubercle bacilli from secretions and excretions, the material is mixed with the citric acid-saponin solution, and centrifuged. An equal amount of 15 or 25 per cent sulphuric acid is added, depending upon the presence of contaminating bacteria. This is permitted to remain for twenty to thirty minutes, when it is neutralized by the addition of the buffer solution until the sediment becomes alkaline to litmus. It is then centrifuged and the sediment planted on the medium.—*Verfahren der Tuberkelbazillenzüchtung aus Blut, Organen, Sekreten und Exkreten, C. Coronini, Zentralbl. f. Bakt., November, 1939, **145:** 24.—(J. D. A.)*

Concentrating Tubercle Bacilli in Sputum.—The sputum is digested by means of the enzyme papain. Approximately 0.5 g. of papain, either in powder form or mixed with a small amount of water to form a paste, is mixed with 50 cc. of sputum. The enzyme-sputum mixture is incubated at 37°C. in either a water bath or hot-air regulator. As soon as complete liquefaction occurs, (average time is ten to fifteen minutes), the mixture is centrifuged at high speed and smears are made from the sediment in the usual way. This method gave a higher average number of organisms per field and a much more even distribution of organisms than by direct smear from undigested sputum. Comparisons with alkali-digested sputum gave practically similar results in 90 per cent of the sputa. In 10 per cent the enzyme digestion method was definitely superior. The above method has the following advantages: digestion of

sputum is rapid, no neutralization is required, the sediment adheres well to glass slides allowing thicker smears, and cultures and animal inoculations may be made from the sediment after appropriate treatment to destroy non-acid-fast organisms, which are not affected by the digestant.—*A Simple Technique for Concentrating Tubercle Bacilli in Sputum, N. P. Sullivan & H. J. Sears, J. Lab. & Clin. Med., July, 1939, 24: 1093.*—(*F. G. P.*)

Negative Sputum.—Since the persistence of positive sputum is considered clear evidence that activity of tuberculosis has continued, at Sea View Hospital a six-months' period of negative sputum has been accepted as essential before consideration of discharge of the patient. Despite the fact that patients with negative sputum have in the past fulfilled all the requirements for discharge, a certain number have reappeared with positive sputum a relatively short time after leaving the hospital. In order to determine whether these readmissions exemplify either endogenous reactivation of their lesions, exogenous superinfection, or persistence of positive sputum without demonstration by ordinary laboratory methods, 41 patients who had fulfilled all the usual requirements for discharge were studied. The sputum specimens of these 41 patients were collected in bottles containing tergitol and the specimens examined according to the method recently described by Petroff and Schain. Of the 41 patients with apparently negative sputum, 13 had acid-fast bacilli by the tergitol method and only 3 of these were positive on guinea pig inoculation. One patient had negative sputum by all usual methods of examination and also by the tergitol method, but gave a positive result on guinea pig inoculation. The fact that only 10 per cent of the patients whose sputum was positive by the tergitol method also had a positive guinea pig cannot be explained at present. The tergitol method is more accurate than other methods in common use and should be used to supplement the usual methods of sputum examination.—*The Apparently Negative Case of Tuberculosis, M. R. Louria & S. Trubowitz, Quart. Bull. Sea View Hosp., April, 1940, 5: 262.*—(*A. A. E.*)

Concentration Methods.—The methods studied were Petroff's, Pottenger's and chemical flocculation (Hanks). The results showed that Pottenger's dilution-flotation method of concentration gives an average of 33 times as many bacilli as can be found in direct smears of choice particles in routine work. The efficiency of this method is twice that of chemical flocculation and four times that of Petroff's. According to Pottenger, this is as accurate as guinea pig inoculation and can detect the presence of as few as 1,000 bacilli in twenty-four-hour collections of sputa, whereas to find tubercle bacilli in a smear by microscopical examination requires the presence of 100,000 tubercle bacilli per 1 cc. of sputum (Corper).—*Evaluation of the Tubercle Bacillus Concentration Methods of Petroff, Pottenger, and Chemical Flocculation, A. H. Nagy, J. Lab. & Clin. Med., October, 1939, 25: 67.*—(*F. G. P.*)

Demonstration of Tubercle Bacilli.—This report involves mainly the comparative results of diagnostic cultures and guinea pig inoculations for the identification of *Mycobacterium tuberculosis* that were run parallel at the Los Angeles County General Hospital over a period of seven years. The specimens used were sputum, negative for acid-fast rods on six smears, urine, faeces, pus and biopsy or autopsy tissue. These were treated with 5 per cent oxalic acid from forty-five minutes to two hours and neutralized with sterile 10 per cent sodium hydroxide using bromthymol blue indicator. Spinal, pleural and peritoneal fluid or pus not containing organisms other than possible *M. tuberculosis* were inoculated as received into cultures and guinea pigs. Herrold's medium was mainly employed for the cultures. The results showed that out of 2,439 tests, 345 were positive by animal inoculation culture, or both methods distributed as follows: guinea pigs positive 301, or 87 per cent; cultures positive 242, or 70 per cent; both cultures and guinea pigs positive 198, or 57 per cent; guinea pigs positive, cultures negative, 103, or 30 per cent; guinea pigs negative, cultures positive, 44, or 13 per cent. Positive results generally appear faster by culture than following guinea pig inoculation. One of the authors (Fisk) developed a method of culturing spinal fluids

which has proved useful in growing out many infectious agents including *M. tuberculosis*. Spinal fluid is centrifuged at high speed for approximately thirty minutes. The supernatant fluid is discarded, and veal infusion broth containing 20 per cent filtered inactivated human serum is poured over the sediment. The tube is tightly corked and incubated. Meningococci, α and β streptococci, staphylococci, pneumococci, *H. influenzae*, diphtheroids, *Coccidioides immitis* and *M. tuberculosis* were recovered by this method. The latter takes two weeks or more to develop gross colonies. These colonies grow in the bottom of the culture and look like little flecks of wax. Neither cultural nor animal inoculation methods were absolutely reliable, and it is suggested that both be performed as a check on one another whenever possible. A simple method for culturing spinal fluid is described. This method favors the growth of many pathogens including *M. tuberculosis*.—*The Diagnosis of Tuberculosis by Culture and Guinea Pig Inoculation, A. Hoyt, F. Holtzwart, B. Kuntzner & R. T. Fisk, J. Lab. & Clin. Med., October, 1939, 25: 88.*—(*F. G. P.*)

Staining Acid-fast Bacilli.—The following method has been used for a year and a half and has been found to be the most reliable means of staining acid-fast bacilli in sections permanently, irrespective of the fixative used. It has been found, however, that its usefulness depends on the quality of the formaldehyde solution used. Washing in tap water after each step being understood, (1) Stain in, New-fuchsin 0.5 g., phenol crystals 5.0 g., alcohol (methyl or ethyl) 10.0 cc. and distilled water to make 100.0 cc., at 60°C. (paraffin oven) overnight for from twelve to twenty-four hours, or at room temperature for from twenty-four to forty-eight hours. The longer periods are recommended for *M. leprae*. (2) Freshly distilled aqueous formaldehyde, 5 to 30 per cent, five minutes. (3) Hydrochloric acid, 2 per cent in 95 per cent alcohol, ten minutes. (4) Potassium permanganate, 1 per cent aqueous, until brown, usually two to five minutes. (5) Oxalic acid 2 per cent, one minute. (6) Harris' haematoxylin, two minutes. (7) Van Gieson's stain, 3 minutes (acid fuchsin 0.1 g., picric acid, 0.5 g. and distilled water to make 100.0 cc.). (8) Without washing, dehydrate in alcohol, clear in xylol, and mount in balsam. Nuclei stain brown, connective tissue fibres red, muscle fibres yellow, and acid-fast bacilli dark ultramarine blue. The preferred fixative is a mixture of equal parts of 10 per cent formaldehyde and 95 per cent alcohol. Fixation for three to five or more days is superior to brief twenty-four hour fixation. The use of formaldehyde of highest purity in the staining process is important. The "reagent" grade of formaldehyde preserved in dark bottles usually is satisfactory, but any commercial formaldehyde, distilled through a simple water cooled glass condenser, gives a usable product containing about 30 per cent formaldehyde. Solutions a few days old are satisfactory, but after three or four weeks, they may become very unreliable. It is advisable to use freshly distilled formaldehyde and to renew it for each batch of slides. By this method lepra bacilli, at times impossible to stain in paraffin sections by other means, have been found to be readily colored.—*The Fuchsin-Formaldehyde Method of Staining Acid-Fast Bacilli in Paraffin Sections, G. L. Fite, J. Lab. & Clin. Med., April, 1940, 25: 743.*—(*F. G. P.*)

Stomach Lavage in Tuberculosis.—The authors present the results of a study of 1,000 consecutive patients who were given stomach lavage in the Chicago Municipal Tuberculosis Sanitarium, 970 of whom were over ten years of age. Of this group, 940 were negative for tubercle bacilli by the routine concentration method, 50 were positive only once, and 10 were positive only twice at the time stomach lavages were done. The latter 60 patients, also found positive by stomach lavage, were used as positive controls. There were 176 negative controls whose clinical and X-ray aspect pointed definitely to a normal status at the time of examination, or to diseases other than lung tuberculosis. All were negative on stomach lavage. Patients are not allowed any food or liquids in the morning, but drink 4 ounces of sterile distilled water before the Ewald tube is passed. Animal inoculations were made in every case, regardless of smear results. There were 253 patients who had been negative for

nine months or longer, by routine examination, although previously positive. Of these, 94 were positive by stomach lavage and 159 remained negative. Of the remaining 511 patients always negative by routine methods, 249 (48.7 per cent) were positive by the stomach lavage method alone. Of the remaining 262 patients always negative, 70 had early minimal or moderately advanced involvement; 79 received pneumothorax therapy; 28 had pleural effusions, and 70 had terminal fibroid lesions where infiltrative foci had disappeared and only stringy fibrosis or fibroid cavities remained. This left only 12 patients to be divided up among a number of complications or unusual features. Of 403 patients with stomach washings positive by guinea pig inoculation, 161 (40 per cent) were positive by smear. Of 824 patients with pulmonary tuberculosis, 334 had some form of collapse therapy, present from two months to several years. Of these 23.7 per cent were never permitted to become positive, 32.9 per cent became negative by stomach lavage, while 43.7 per cent were still positive by stomach wash. Of 940 patients, therefore, negative on direct examination, 249, or 26.5 per cent, were found positive only by stomach lavage. Deducting the controls and the patients at one time positive, this represents an efficiency value of 48.7 per cent for the lavage method. Completely healed tuberculous lesions and nontuberculous diseases are uniformly negative by stomach lavage. As stomach lavage seems to come nearer than any other method to finding all virulent tubercle bacilli, it should be adopted as the ultimate standard for absolute negativity or apparent cure of patients having had or suspected of having tuberculosis. It is an excellent method to control the efficiency of collapse therapy. For accurate information the washings must be repeated at frequent intervals, especially when the collapsed lung is reëxpanding. No patient with clinical signs of tuberculosis but negative sputum should be considered negative until lavage has yielded negative results.—*Stomach Lavage in the Diagnosis and Control of Treatment of Tuberculosis, A. Stadnichenko, S. J. Cohen & H. C. Sweany, J. A. M. A., February 24, 1940, 114: 634.*—(*G. L. L.*)

Fluorescent Microscopy.—The method of Keller was used, with a 2:1000 solution of Auramine. In 200 examinations of material already known to be positive by the Ziehl-Neelsen method, the fluorescence method gave the same positive results, but required less time for the examination of the slides because a larger microscopical field could be covered by the use of small power objectives, i.e. 10x or 20x. In 241 examinations of previously negative material, 7 per cent were positive by the Ziehl-Neelsen method, 18.7 per cent by the fluorescence method, and 34 per cent by culture on Petragnani's medium or by guinea pig inoculation. This method is time-saving, more accurate and economical, because in less than 50 per cent of cases biological proof is needed. Occasional doubtful results may be had with the fluorescence method, but this is also true of the usual staining methods.—*L'uso del microscopio a fluorescenza nella ricerca del bacillo di Koch, B. Besta, Ann. d. Ist. Carlo Forlanini, November–December, 1939, 3: 904.*—(*S. L.*)

Fluorescent Microscopy.—A method of staining is described which allows an improved demonstration of tubercle bacilli in histological sections. The procedure is based on the typical aspect of the bacilli in the fluorescent light when treated previously with Auramine. A fluorochrome such as thiazol-yellow is used as counterstain. The staining takes about twenty minutes. Sections which had been recently stained with haematoxylin or van Gieson may be easily decolorized and restained. The technique can be used for either paraffin or frozen sections. Elastic fibres and cholesterin are known to give a similar fluorescence. The color and shape of the tubercle bacillus, however, should allow the differentiation without difficulties. Particles of tissue which were previously treated with antiformin or material that has been in formalin longer than four or five days are not suitable. The method is recommended though the experiences so far are based on a limited number of cases.—*Vereinfachter Nachweis von Tuberkelbazillen in histologischen Schnitten durch die Fluoreszenzmethode nach Hagemann, G. Schallock, München. med. Wchnschr., January 26, 1940, 87: 102.*—(*A. B. T.*)

Fluorescent Microscopy.—The advantages of the fluorescent microscope in demonstration of tubercle bacilli have been previously reported. There is considerable saving of time and less fatigue. In a series of 1100 examinations there were 22.7 per cent more positive results with the fluorescent microscopy than with the Ziehl-Neelsen method. Negative in relation to positive results were: for sputum 3:4 with Ziehl-Neelsen and 3:5.5 with the fluorescent microscopy; for antiformin concentration 3:0.9 and 3:1.4; for gastric juice 9:1 and 8:1. The use of the method in the tuberculosis hospital is highly recommended, but it cannot replace culture and animal experiments.—*Fluoreszenzmikroskopie und Tuberkelbazillennachweis im Tuberkulosenkrankenhaus, P. P. Schneider, Ztschr. f. Tuberk., May, 1940, 84: 319.*—(*G. C. L.*)

Fluorescent Microscopy.—The author reviews the literature and his own experience with the fluorescent microscope in the finding of tubercle bacilli in the sputum. Out of 530 examinations with the fluorescent microscope the author had 110 positive results; out of 530 examinations with a staining method (Jötten Haarman), 100. In the large tuberculosis laboratory the fluorescent microscope has a distinct advantage over the usual staining methods, which is, however, not true for individual examinations.—*Wie hoch ist der Gewinn an positiven Tuberkulosepräparaten durch das Fluoreszenz-Mikroskop? H. Gärtner, Ztschr. f. Tuberk., September, 1939, 83: 27.*—(*G. C. L.*)

Fluorescent Microscopy.—Fluorescent microscopy has been employed as an alternative method of identifying tubercle bacilli on the slide. The preparation is stained with Auramine, a yellow anilin dye; when viewed under the microscope, the organisms are colored a yellowish green. In order to determine the accuracy of this method, 702 specimens, including sputum, pus, urine, faeces and other body fluids of suspected tuberculous nature, were examined. These were examined for tubercle bacilli by four methods: animal inoculation, culture (according to the method of Löwenstein, Lockemann and Hohn), Ziehl-Neelsen stain and Auramine stain according to the method of Hagemann. Altogether there were 157 positive specimens. One hundred and twenty-nine were positive by the Ziehl-Neelsen method, 137 by the Auramine method; 12 were discovered by cultural methods and 8 were uncovered only by animal inoculation. Of the 157 positive specimens the following figures show the percentage accuracy of the various methods: animal inoculation, 100; culture, 92; Auramine, 87.2; Ziehl-Neelsen, 82.2. Of the staining methods the Auramine fluorescence method is not only somewhat more accurate but is also definitely time saving particularly in searching for tubercle bacilli in tissue preparations.—*Über den fluorescenzmikroskopischen Nachweis von Tuberkelbakterien, H. Didion, Klin. Wchnschr., October 7, 1939, 18: 1315.*—(*H. R. N.*)

Effect of Sulfapyridine on Tubercle Bacilli.—Sulfapyridine added to glycerol broth in concentrations of 1:1000 and 1:2000 prevented growth of tubercle bacilli. Concentrations of 1:4000 retarded growth and 1:6000 and 1:10000 had little or no effect.—*Effect of Sulfapyridine upon Growth, in vitro, of Tubercle Bacilli, H. Green, Proc. Soc. Exper. Biol. & Med., February, 1940, 43: 344.*—(*F. B. S.*)

Effect of Chlorophyll Derivatives on Tubercle Bacilli.—Chlorin-e, prepared by splitting off the magnesium atom from chlorophyllin, and chlorophyll in concentrations of 0.025 and 0.050 per cent in glycerine broth and Sauton's media inhibited the growth of H 37 and avian type tubercle bacilli, but copper chlorin-e, deuteroporphyrin, copper deuteroporphyrin and pyrroporphyrin sulfonic acid-sodium-salt did not. The tuberculoprotein of the living bacillus seems to be capable of binding copper chlorin-e, probably in chemical union, as indicated by the absorption spectrum.—*Effect of Chlorophyll Derivatives and Related Compounds on the Growth of M. tuberculosis, S. Daly, G. Heller & E. Schneider, Proc. Soc. Exper. Biol. & Med., October, 1939, 42: 74.*—(*F. B. S.*)

Sulfanilamide and Growth of Acid-fast Bacilli.—Previous experiments are cited (1938) in which some inhibitory effect of sulfanilamide

in certain specified concentrations was observed on the growth of human tubercle bacilli *in vitro* and the present observations are a continuation along the same line of work, bovine and avian, as well as smegma bacilli, being included. Both nutrient egg-agar medium and synthetic egg medium were employed, at a pH of 6.8 and 6.2, respectively. Three strains of virulent human tubercle bacilli were used, including one seeded directly from treated sputum, the bovine and avian strains were from Trudeau, New York, and the smegma from H. J. Corper of Denver, Colorado. The media used had sulfanilamide added in concentrations varying from 1-1000 to 1-10,000. Measured small quantities of bacillary suspensions of known strength and age were used for seeding. Some retardation in inhibition of growth in tubes containing the stronger concentrations of sulfanilamide was noted, very little on those with the weaker. It is concluded that under specified conditions and in certain concentrations sulfanilamide exerts an inhibitory effect upon the growth of acid-fast bacilli *in vitro* but that the results to date do not permit of clinical application.—*The Action of Sulphanilamide upon the Growth of Acid-fast Bacilli in vitro, H. C. Ballon & A. Guernon, Tubercle, February, 1940, 21: 153.* —(*A. P.*)

Effect of Sulfonamides on Tubercle Bacilli.—Sulfapyridine and prontosil rubrum caused greater inhibition in the growth of 14 strains of mycobacteria in Sauton's medium than did sulfanilamide. Significant inhibition was caused by 10 mg. per cent concentration of sulfapyradine and prontosil, whereas 90 mg. per cent concentration of sulfanilamide was necessary to effect the same amount of inhibition. Growth was determined by weight.—*Bacteriostatic Effect of Sulfapyridine, Sulfanilamide and Prontosil Rubrum in vitro on Mycobacterium, K. E. Birkhaug, Proc. Soc. Exper. Biol. & Med., October, 1939, 42: 275.*—(*F. B. S.*)

Koch Bacillus in the Nontuberculous.—The action of the Koch bacillus, after it invades the human body, is usually limited to the formation of small latent lesions, called the primary infection or reinfection, depending upon whether this occurs in a person free from tuberculosis or in an individual who has had a previous infection. Only in a small number of cases does this invasion cause a clinically apparent tuberculosis. The authors felt that a study of the virulence of the latent lesions found in the adult patients whose death was not due to tuberculosis would prove of interest, both from a bacteriological and a pathological point of view. This work not only included a study of the latent lesions but also of the grossly normal tissues. Of 207 specimens of tissue taken from 90 patients only 184 gave positive or negative results. All cases with the exception of 8 were over forty years of age and the greater number of these were over sixty years. All cases were free from any known clinical tuberculosis. Some difficulty was encountered in distinguishing between the calcified chancre and the calcified nodule of reinfection but this was solved by the study of the satellite lymph nodes which presented calcifications in the former lesion but were absent in the latter. Inoculations gave 38 positive and 61 negative results, while by culture they obtained 11 positive and 70 negative results, and 18 contaminations. When the culture was positive, the animal inoculation was always positive but in 20 cases with positive inoculations the cultures were negative. The paucibacillary character of some of the lesions was manifested in some of the animals by the lack of generalization of the lesions as late as seventy days after inoculation, by the absence of tuberculinization in spite of the prolonged survival period and by the long ante-allergic period fifty to seventy-seven days). These show that it is not a question of attenuation of the bacilli because they also found that the virulent titre of several strains obtained from the specimens was the same as that possessed by the human bacillus. Of the 11 apical and subapical caseous and cretaceous nodules studied, 7 were positive and 4 were negative for tubercle bacilli. This demonstrated to them that bacilli can disappear from tuberculous lesions at an early period. The calcified primary and reinfection lesions gave 11 positive and 33 negative findings out of 44 animal inoculations. Of the 34 apical fibrous nodules, probably due to tuberculosis, there were 6 positive and 28 negative results.

Sixty inoculations of liver and spleen from 10 cases with definite tuberculous changes in the lungs or mediastinal lymph nodes were all negative. Specimens of normal lung tissue were removed from 18 cases, of which 14 cases presented scars of pulmonary tuberculosis, and of these scars 5 contained virulent tubercle bacilli, 9 of the cases contained virulent bacilli in the mediastinal lymph nodes, however, only one specimen of the 18 presented a positive inoculation. A pulverized mixture of fragments of grossly nontuberculous mediastinal lymph nodes taken from 40 adults, with and without anthracosis, resulted in 26 positive animal inoculations. In addition, a pulverized mixture of both grossly normal and calcified mediastinal lymph nodes of 26 cases gave 15 positive and 11 negative findings for tubercle bacilli. The authors here point out the close similarity of positive results in the latter two experiments as against the finding of only 20 per cent positive inoculations obtained from isolated calcified lesions, and conclude from this that in the majority of instances the bacilli come from the grossly normal nodes. In addition they point out that in many instances in the latter experiments a torpid form of tuberculosis was encountered in the inoculated animals, showing the paucibacillary character of the material. From the above research the authors conclude that there is a strong tendency for sterilization of the clinically latent lesions. They cannot give the exact site of the tubercle bacilli in the lesions but because nutritive exchanges are known to take place between the centre of a lesion and the surrounding blood supply, as can be surmised from the change of the soft centre of some lesions with a calcified periphery to complete ossification, they believe that the bacillus can survive in the centre as well as the periphery. The sterilization of a tuberculous lesion is a function of its histological maturation. The rapidity of scar formation diminishes with age, and so the lesions of older patients are histologically less advanced than the similar lesions found in younger persons and therefore are more likely to remain virulent for a longer time. Sixty per cent of the tracheobronchial nodes of the adults studied revealed the presence of tubercle bacilli, and these nodes were almost always grossly normal. The bacilli thus found were always attenuated. Pulmonary scars were often sterile in those people who harbored the bacilli in the macroscopically normal nodes. The bacilli in these nodes come apparently from contaminations distinct from those causing the parenchymal infections, that is, the human body can harbor tubercle bacilli other than those of the primary infection. The bacilli of reinfection are to be seen in the normal nodes of more than 40 per cent of the adults autopsied and they feel that this figure can be increased with extensive research. They are unable to exclude the presence of the bacilli of reinfection in patients who are still carriers of the bacilli of the primary infection and in cases where the possibility of reinfection can recur the presence of both is very likely the rule. The persistence of the tuberculin sensitivity in adults is not due to the persistence of the virulence of the primary infection, considering the progressive sterilization of the tuberculous lesions, but rather due to the successive reinfections. It is through a series of tuberculous reinfections that the authors explain the persistence of the tuberculin reaction. However, numerous reinfections are not necessary for this cycle because sterilization of a lesion in children requires many years and also because the rapidity of sterilization diminishes with age.—*Recherches sur la sort du bacilli de Koch chez la sujets cliniquement non tuberculeux, A. Saenz & G. Canetti, Ann. Inst. Pasteur, April, 1939, 62: 361.*—(*M. A. B.*)

Tubercle Bacilli in Milk.—The authors present a study of samples of commercial products taken from different sections of Paris, particularly from the smaller retailers in well populated districts where some of the products sold, especially butter, are often of an inferior grade. Of the 45 specimens of milk examined both by inoculation and culture, no tubercle bacilli were found. However, one specimen contained a nonvirulent paratubercle bacillus. Only one of 22 specimens of butter presented a growth of a bovine type of tubercle bacillus. Fifteen samples of cheese were all negative for tubercle bacilli. Four of the 22 specimens of cream contained the bovine type of tubercle bacillus. Of the 8 samples of yoghourt only one con-

tained a virulent form of bovine tubercle bacillus. The authors conclude that the milk and its products are apparently sufficiently pasteurized. The authors also found that the isolation of the tubercle bacillus from cream and butter can be carried out by the inoculation into the guinea pig of the centrifuged residue, but the fatty matter must be destroyed after centrifuging, otherwise the animals may die prematurely. They caution against early sacrifice of animals, since the growth and formation of the tuberculous lesions are usually very slow due to the small number of bacilli encountered in the specimens. All cultures were negative.—*Recherches sur la présence du bacille tuberculeux dans le lait et les produits derivés, A. de Grolier & T. Voiculesco, Ann. Inst. Pasteur, August, 1939, 63: 145.*—(*M. A. B.*)

Virulence of Tubercle Bacilli.—Subcutaneous injection of tubercle bacilli in the mouse causes an occasional infection, even when strong doses are used, whereas an intraperitoneal injection produces a progressive and fatal tuberculosis. Mice may also be infected by ingestion as well as by inhalation, but the intraperitoneal and especially the intravenous routes offer the greatest possibility for a positive result. The cerebrospinal tract also offers a means of infecting white mice. Attenuated strains of tubercle bacilli do not provoke the formation of any lesions by these routes. Laboratory strains which have some virulence for the guinea pig and the rabbit sometimes show slight pathogenicity for mice. The mouse does not react to tuberculin because it is not sensitive to the toxic action of the tubercle bacillus. Using freshly isolated strains of bacilli, white mice were inoculated with various strains of the human, bovine and avian types. It was found that white mice are resistant to tuberculosis. Weak doses of bacilli, 10^{-5} mg., of any type of tubercle bacillus never causes a rapid and fatal disease but stronger doses, ranging from 0.1 to .01 mg. of virulent bacilli are constantly fatal. The human strains of bacilli not virulent for the guinea pig are also not virulent for mice. Strains having equal virulence for guinea pigs, showed variations of virulence when injected into mice. These differences correspond to real and intrinsic differences of the strains used. Mice were found to react in a constant manner to the bovine strains and it is for this reason that it is possible to find the titre of virulence of these types. The avian type of bacillus is much less virulent for mice than the mammalian types. The avian bacillus kills the mouse only after a long period and the pulmonary lesions become manifest only after the disease has existed for at least two months. Thus the inoculation of a strain of tubercle bacillus into mice permits one to determine whether or not the strain belongs to the avian type, both by the course of the disease and the lesions produced. The course of the disease and the lesions produced in white mice by the inoculation of strong doses of either the human or the bovine strains are similar. If .001 mg. of either type of bacillus was inoculated into white mice through the intravenous route, it was found that the bovine strain provokes a progressive and a rapidly fatal disease, while the human strain generally causes a more benign type of disease. They postulate that if at least 2 out of 4 mice inoculated with .001 mg. of bacilli die with nodular tuberculosis of the lungs and the other organs and all lesions contain a large number of bacilli, then the bacilli belong to the bovine type.—*Virulence des trois types de bacilles tuberculeux pour la souris blanche, N. Stamatin & L. Stamatin, Ann. Inst. Pasteur, September, 1939, 63: 269.*—(*M. A. B.*)

Effects of Acid-Alkaline Variations and Pathogenicity of Tubercle Bacilli.—Smithburn's experiments have been concerned with variations induced solely by alteration of the pH of the culture medium. He had previously found that the colonial morphology could be markedly influenced by control of the pH and that nongranular, smooth colonies were most numerous when it was adjusted to pH 6.8, contrasting with the coarsely granular irregular ones when it was adjusted to pH 6.0. Flat, spreading, finely granular colonies were characteristic of growth on medium of pH 7.2, while intermingled forms occurred at pH 6.4. This report is concerned with the pathogenic properties of these four lines of culture. The

bacilli used were originally derived from a single bovine strain 39, isolated by Theobald Smith and grown on Corper's glycerolated egg-yolk medium adjusted by addition of phosphate buffers prior to inspissation. Virulence tests were made by inoculation of standard doses of organisms from the third, fifth and seventh generations grown at pH 6.0, 6.4, 6.8 and 7.2. Suspensions were prepared so that 1.0 cc. contained 1.0 mg. (moist weight) of organisms. Rabbits were inoculated intravenously with 1.0 cc. of inoculum containing the desired dose. Guinea pigs were inoculated intracerebrally under ether anaesthesia by a specially described method. The dose for guinea pigs was between 0.000,001 and 0.01 mg. given in 0.1 cc. saline diluent. Blood counts were made on the 40 rabbits before and at weekly intervals after inoculation. Colonies cultivated at pH 6.0 proved coarsely granular and markedly attenuated, the lesions produced being of the "hard," noninvasive type, with little tendency to caseation. The optimum growth point for smooth colonies was pH 6.8 and these were highly virulent, producing acute or "soft" tubercles, massive and caseating. Those grown at pH 6.4 were moderately attenuated; at pH 7.2 slightly so, some of these forms inducing acute type lesions. Attenuated organisms appeared to be destroyed by the tissue cells but the virulent ones apparently destroy the polynuclear and mononuclear phagocytes and multiply rapidly. Valuable prognostic information was afforded by the studies of the monocytes, lymphocytes and monocyte-lymphocyte ratio which rises with progression of the disease.—*Acute or Chronic Tuberculous Lesions as Produced by Colonial Variants of Tubercle Bacilli, K. C. Smithburn, Tubercle, June, 1939. 20: 420.*—(*A. P.*)

Pathogenicity of BCG after Prolonged Cultivation.—Calmette and Plotz in 1929 stated that this strain of tubercle bacilli is definitely and permanently innocuous. However, they recommended its cultivation on glycerin-broth-potato with a change at intervals to glycerinated oxbile potato. In this experiment continuous cultivation on glycerinated egg medium was used in an attempt to increase pathogenicity. Previous experiments by others have indicated that under these conditions BCG could induce lesions of a tuberculous character but not a progressive tuberculosis that is reinoculable. They failed to indicate a significant increase in virulence. A twenty-three day old culture representing the fifty-ninth generation of growth on glycerinated egg media, having a rough pebbly contour, with little chromogenesis, was inoculated into 12 guinea pigs and 18 rabbits. In all cases, 2 mg. moist weight was used. The animals were carefully separated from those in whom ordinary tubercle bacilli had been inoculated. The experiment was continued for fifteen months, at the end of which time 3 guinea pigs and 13 rabbits were still living. No instance of progressive malignant disease was recorded although nonprogressive morbid visceral lesions were observed. Injection of tissue emulsions into other animals uniformly failed to produce tuberculosis. Most characteristic lesions were epithelioid tubercles without necrosis. Nine of the 16 living animals reacted to tuberculin, usually mildly. Lesions were present in 4 which failed to react.—*The Pathogenicity of BCG after Prolonged Cultivation on Glycerinated Egg Medium, W. H. Feldman, Tubercle, March, 1939, 20: 253.*—(*A. P.*)

Blood Constituents and Growth of Tubercle Bacilli.—Evidence from growth experiments seems to show that haemoglobin inhibits surface growth of tubercle bacilli but permits slow depth growth in a liquid medium. Such inhibition passes off after a large part of the haemoglobin is destroyed. Viability experiments show that tubercle bacilli die less rapidly in citrated normal human blood than in distilled water, 0.9 per cent saline and in Long's medium of pH 7.2. Haemoglobin, though inhibitory for growth, has no direct bactericidal action on tubercle bacilli. Differences in culture *in vitro* and *in vivo* are considered as possibly modifying these results. The constant renewal of circulating haemoglobin *in vivo*, however, probably increases the inhibitory effects.—*The Influence of Normal Blood and Certain of Its Constituents on the Growth and Viability of the Tubercle Bacillus, R. Davies, Tubercle, Supplement, May, 1939, 5.*—(*A. P.*)

Growth of Tubercle Bacilli in Serum.—About 90 per cent of sera obtained from normal persons and patients with bronchogenic phthisis restricted to the lungs support growth of tubercle bacilli in the depths of glycerol peptone water or in Kirchner's medium, whereas approximately 70 per cent of the sera obtained from patients with chronic disseminated tuberculosis fail to support growth. The failure to support growth is more pronounced in sera obtained from active cases than in those from inactive cases, but does occur irrespective of the activity of the patient's lesion. Serum which has failed to support growth can be made to do so by absorption with acid-fast organisms or with *B. coli*. This effect is not due to the introduction of a growth-promoting factor, or to an action upon complement, but is produced by the absorption of a growth-inhibiting factor. Vaccination of rabbits and guinea pigs with heat-killed tubercle bacilli does not affect the growth-promoting power of their sera.—*The Effect of Blood Serum on the Growth of Tubercle Bacilli in the Depth of Liquid Media, W. Pagel, J. Path. & Bact., January, 1940, 50: 111.*—(*H. J. H.*)

Vitamins and Growth of Tubercle Bacilli.—In 1927 Nao Uyei observed that while cod-liver oil did not influence growth of the tubercle bacillus *in vitro*, lemon juice and brewers' yeast had an intensely stimulating action on its growth. Leither in 1937 found that ascorbic acid and vitamin B_1 would favor the growth of the tubercle bacillus when used in small doses, and inhibit it when larger doses were used. Boissevain, Heise and others also reported similar experiences. From the biological standpoint it appears that vitamins exert a catalytic action on cellular metabolism, which is comparable to that of enzymes. It is logical to think that every vitamin possesses a peculiar mode of action. The action of vitamin B_1 is closely connected to carbohydrate metabolism, and that of vitamin C to the processes of oxidation and hydrogenation of organic cells; vitamin D greatly increases cellular functions. Savagnone planned to find the optimum dose of each of these vitamins, and for his research chose the Kirchner medium, to which he added 10 per cent of blood serum; pH was constantly determined at 6.9. This sterile medium was distributed in culture tubes, 20 cc. in each tube. Different vitamins, in various amounts, were added to some of the tubes, while a certain number of tubes with the plain medium were used as controls. Then an equal quantity of a known strain of human tubercle bacilli was inoculated to every culture tube, and all tubes were placed in an incubator at 37°C. Bacterial growth did not start sooner when adequate doses of vitamins were added to the medium, but it was somewhat retarded by higher doses. Bacterial growth went on faster and was more luxuriant in the tubes with vitamin C, a little less in the tubes with vitamin B, but always more than in the control tubes. Vitamin D had no influence on the cultural growth. Activating action of both vitamins, B and C, was in direct relation to their dosage, becoming weaker, and even disappearing, when optimum dosage was surpassed. Specificially, these optimum doses were found to be 2 drops of orange or lemon juice, 3 drops of tomato juice, and 3 drops of a 2 per cent aqueous solution of brewers' yeast, when added to 20 cc. of the modified Kirchner medium. Experiments carried on with synthetic vitamins, cebion and betabion, gave the same results as with vitamins C and B.—*Influenza di alcune vitamine sullo sviluppo colturale del microbatterio tubercolare, L. Savagnone, Gior. di batteriol. e immunol., April, 1940, 24: 408.*—(*S. L.*)

Chemical Factors in Growth of Tubercle Bacilli.—Since certain metal ion catalysts which caused enhanced growths of tubercle bacilli are also known to accelerate the rates of oxidation of biological and simple thiol systems it was felt that it would be of interest to study the effect of diphenylamine which is known to act as an inhibitor of oxidation. Kharnsch and others found previously that diphenylamine profoundly influenced the growth of various bacteria on different media. This remarkable effect is in accord with the results obtained in the authors' laboratory with tubercle bacilli in all of the media used. The work of Kharasch and others with *Staphlococcus aureus* was repeated and extended and concurrent comparative studies were carried out

with bovine tubercle bacilli (B599). The preliminary studies were carried out with nonsynthetic media. A large number of experiments were done using a number of inhibitors on a bovine (B599) and a human strain (H37) of tubercle bacilli, employing ordinary "C.P." as well as "highly purified" media. The data are not sufficient to draw far-reaching conclusions, yet they indicate that on "highly purified media" the bacteria are much more sensitive to the action of the inhibitors than on media containing ordinary "C.P." reagents. In some cases the results are most striking for a ten-fold difference in effect was observed in the case of catechol. On a 2 per cent "C.P." agar medium it prevents growth in 1:5,000, and on the "highly purified media" it prevented growth in 1:50,000. In other cases the results were less outstanding yet the trend was unmistakable. Thus, instead of a ten-fold effect, only a three-fold effect was observed with a number of other hydroxy compounds. Strikingly, the diphenylamine series of compounds shows no difference in inhibiting power in "highly purified" and normal media. These results are highly suggestive, but it is fully realized that further data are needed to evaluate the factors responsible for the results. It is of considerable interest that these antioxidants have a tremendous inhibitory power on bovine, and in particular on human strains of tubercle bacilli. The tremendous inhibitory effect observed, for instance, on H37 in which growth was prevented by diphenylamine in 1:50,000 concentration as compared to 1:2,000 necessary to prevent growth of *Staphylococcus aureus* is highly suggestive. Summary: The diaryl secondary amines investigated were uniform in their activity regardless of whether "C.P.," "Purified" or nonsynthetic medium was used. Each of the dihydroxybenzenes and the aryl-aliphatic secondary amines was more effective in "Purified" medium than in "C.P." or meat broth medium. Some of the aryl-aliphatic secondary amines and dihydroxybenzenes were more effective than the diaryl secondary amines in "Purified" medium. In the "C.P." or meat broth medium they were less effective. A number of antioxidants were tested for their inhibiting effect on the growth of tubercle bacilli. No attempt has been made at this time to correlate the oxidation-reduction potential or "apparent" oxidation-reduction potential of these materials and their effectiveness in inhibiting the growth of tubercle bacilli. This work is being continued.—*Chemical Factors Influencing the Growth of Tubercle Bacilli, II. Organic Reagents, B. C. Sher & H. C. Sweany, J. Bact., October, 1939, 38: 411.*—(*F. G. P.*)

Growth of Tubercle Bacilli.—It is generally believed that tubercle bacilli will not grow on synthetic media when less than 10^{-1} mg. of bacilli are planted. It is also a general belief that they must be planted on the surface of the liquid medium for growth to occur; that if they sink beneath the surface they do not multiply. Agar when combined with synthetic media has been assumed to be inert toward the growth of tubercle bacilli. In the present study these beliefs were investigated using a slightly modified Long's synthetic medium and U.S.P. quality agar in a granular form. The results show that human tubercle bacilli of the strain H37 and of a subcolony strain of the latter will grow in a synthetic medium when amounts at least as small as 10^{-6} mg. are planted in it. These bacilli grow on the bottom of the synthetic medium and later there is growth on the surface. Agar is definitely inhibiting to the growth of these bacilli when amounts greater than 0.1 or 0.25 per cent are added to the synthetic medium and less inhibiting when smaller amounts are used. Colonies of these bacilli can be grown at different levels of 0.1 per cent agar in the synthetic medium. The above facts will be of value in the study of probable accessory growth factors for tubercle bacilli.—*The Growth of Human Tubercle Bacilli H37, in Synthetic Medium with and without Agar, W. F. Drea, J. Bact., February, 1940, 39: 197.*—(*F. G. P.*)

Metabolism of Tubercle Bacillus.—The growth of a human type strain tubercle bacillus paralleled the consumption of glycerol and other constituents of the Long's synthetic medium upon which they grew. The glycerol was completely consumed at the end of 3.5 weeks, at which time occurred the maximum weight of bacilli. Thereafter rapid autolysis

appeared. No lactic acid was formed.—*Metabolism of the Tubercle Bacillus in Long's Synthetic Medium, T. E. Friedemann & Florence B. Seibert, Proc. Soc. Exper. Biol. & Med., December, 1939, 42: 41.—(F. B. S.)*

Analysis of Tubercle Bacillus.—Among the biological reactions important in the interpretation of tuberculosis, anaphylaxis and allergy have been confused variously because of the close similarity of some of their manifestations, while a third, specific immunity has been likened to allergy and has been considered the manifestation of the same phenomenon. The experimental solution of these bio-immunological phases of tuberculosis has been hampered in the past because pure natural products were not available until recently when simple nonprotein media were devised and satisfactory adequate aseptic methods of filtration and concentration became available for use. In the present study the aseptic natural filtrate from the growth of human tubercle bacilli on a simple nonprotein synthetic medium and the human tubercle bacilli themselves were used to study these immunological phases of tuberculosis. The results show that on a simple synthetic nonprotein medium (Wong-Weinzirl, 500 cc.) maximum bacillary growth occurs within two to three months, while tuberculoprotein liberation into the medium takes place mainly after maximum growth is attained. The bacillary body sensitizes primarily to tuberculo-allergy and serves to immunize against virulent infection, while the natural filtrate containing tuberculoprotein sensitizes to anaphylaxis and provokes anaphylactic shock and allergic intoxication but does not sensitize to allergy nor specifically immunize against virulent infection. Tuberculo-anaphylaxis, tuberculo-allergy and tuberculo-immunity show distinctive characteristics which lead to the conclusion that they are separate and apparently unrelated biological phenomena.—*Analysis of the Tubercle Bacillus and Its Natural Products by Immune, Allergic, and Anaphylactic Tests, H. J. Corper, J. Infect. Dis., January-February, 1940, 66: 23.—(F. G. P.)*

Lipids of Leprosy Bacillus.—After the so-called leprosy bacillus had been exhaustively extracted with alcohol-ether and chloroform, 19.2 per cent more lipids could be extracted after the cells were treated with dilute hydrochloric acid. The least soluble of three main lipid fractions gave, on saponification, 40.5 per cent carbohydrate and 66.4 per cent ether-soluble compounds. The latter were mainly optically active hydroxy acids, similar to leprosinic acid, and a small amount of lower fatty acids, and unsaponifiable or neutral material, which contained d-eicosanol-2 and d-octadecanol-2. When the hydroxy acid was heated *in vacuo* to 250–270°, volatile crystalline acids could be distilled off, among which was a crystalline tetracosanoic acid, m.p. 76–77°.—*The Chemistry of Lipids of Tubercle Bacilli. LVIII. Concerning the Firmly Bound Lipids of the So-Called Leprosy Bacillus, W. B. Geiger, Jr. & R. J. Anderson, J. Biol. Chem., December, 1939, 131: 539.—(F. B. S.)*

Synthesis of Phthiocol.—A method for obtaining prismatic yellow crystals of phthiocol from crude dry quinone is described. The quinone was treated with calcium hypochlorite containing active chlorine, heated with strong sulfuric acid, dissolved in ether and then extracted with 5 per cent potassium hydroxide, acidified and recrystallized from methyl alcohol. It had the correct melting point of 173–174°C. and the yield was 57 per cent of the theoretical.—*Concerning the Synthesis of Phthiocol, (Letter to the Editor), J. Biol. Chem., September, 1939, 130: 429.—(F. B. S.)*

Mycolic Acids of Avian Tubercle Bacilli.—The two principal hydroxy acids of high molecular weight found in the avian tubercle bacillus wax have been named avian α- and β-mycolic acid. The avian α-mycolic acid decomposes when heated to 210–255°F. under 1 mm. pressure, and a branched chain pentacosanoic acid, $C_{25}H_{50}O_2$, m.p. 78–79°F., distils off in a yield of 25 per cent. The β-mycolic acid decomposes when heated to 280–295°F. under 1 mm. pressure and yields 21 per cent of normal tetracosanoic acid, $C_{24}H_{48}O_2$.—*The Chemistry of the Lipids of Tubercle Bacilli. LVII. The Mycolic Acids of the Avian Tubercle Bacillus Wax, R. J. Anderson & M. M. Creighton, J. Biol. Chem., July, 1939, 129: 57.—(F. B. S.)*

Polysaccharide of Lipids of Leprosy Bacillus.—The polysaccharide isolated from the firmly bound lipids of the leprosy bacillus consists principally of pentosans, and d-arabinose is the chief constituent. There are also 7 per cent of other pentoses and a small amount of d-galactose. The sugars actually isolated account approximately for the total amount of reducing sugars liberated on complete hydrolysis, but represent only about one-half of the polysaccharide.—*The Chemistry of the Lipids of Tubercle Bacilli. LIX. The Composition of the Polysaccharide of the Firmly Bound Lipids of the Leprosy Bacillus, R. J. Anderson & M. M. Creighton, J. Biol. Chem., December, 1939, 131: 549.*—(*F. B. S.*)

Dissociation of Tubercle Bacilli.—Dissociation of tubercle bacilli has been studied in most cases merely by using laboratory material, and seldom has it been correlated with clinical manifestations. For this research pus was collected from fluid cold abscesses and the succeeding stages of dissociation of the bacilli, as isolated by culture on Petragnani's media, were correlated with the clinical evolution of the abscesses. Cultures were always examined after the first inoculation and the purulent material was always withdrawn aseptically from the abscesses. This pus was never treated with sulfuric acid or with sodium hydroxide; 1 cc. of it was directly inoculated into each of three tubes containing the Petragnani's medium. Tubercle bacilli that were isolated from these osteoarthritic abscesses presented characteristics that were related to the developmental period of the abscess. Bacilli isolated from early abscesses, when the pus is creamy and yellow, had colonies presenting the fundamental appearance of S-strain; while when the pus was bloody and caseous, from lesions typically chronic and tending to resolution, colonies appeared as an R-strain. By following the evolution of the process in given abscesses, a gradual process of dissociation of the bacilli was noted in favorable cases, parallel to gradual healing. This may denote a relation between the phenomenon of dissociation and the anatomico-clinical course of the abscess. A correlation between the general course of the disease and the local manifestations could not, however, be made evident either as to quality of pus, or as to character of colonies. This may explain dissociation rather as a result of local factors than as a result of the general infection. Rich cultures were usually obtained in all cases studied, some showing a luxuriant growth in little over two weeks, while others had isolated and discrete colonies, always in less than a month's time. All cultures had similar characteristics: growth occurred always on the surface, never through the thickness of the medium; the colonies were always individually distinct, though more or less close together, even when of R-strain. In successive transfers the colonies tended constantly to change from S to R, more or less rapidly, but in such a manner as to permit the author to follow the course of dissociation in the first cultures only. It appears from this study that dissociation of the tubercle bacillus strain from S to R is possible, and that it is related to the corresponding evolution of the osteoarthritic process toward chronicity.—*Il bacillo tubercolare nelle forme osteoarticolari studiato dal punto di vista dissociativo, R. Marconi, Gior. di batteriol. e immunol., December, 1939, 23: 782.*—(*S. L.*)

Bovine and Human Strains of Tuberculosis.—Bertrand and his coworkers inoculated rabbits' brains with a suspension containing one-twentieth of a milligram of tubercle bacilli and observed that bovine tubercle bacilli induced a paralysis which began in seven to fourteen days after injection and progressed until the death of the animal on the twentieth to the thirtieth day. At autopsy such animals had local brain lesions and manifested the dissemination of the bovine type organisms by extensive lung and visceral lesions. Human strains caused no sign of disease, and only traces of scar tissue could be observed at the site of inoculation when the animals were killed and examined. The authors inoculated a series of rabbits in an attempt to apply this method to the type differentiation of cultures. The results showed that the reaction of the bovine strain of *Mycobacterium tuberculosis*, when inoculated into the brain of rabbits, is not unique since 19 strains, obviously human in origin and proved to be the human type by

intravenous inoculation, induced symptoms like those produced by known bovine strains and described by Bertrand, Bablet and Block. It would appear unwise to discard hastily the classic technique of intravenous injection in order to differentiate the bovine from the human type of *Mycobacterium tuberculosis.*—*The Differentiation of Bovine and Human Strains of Tuberculosis by the Method of Bertrand, Bablet and Block, M. Beattie & R. Nicewonger, J. Lab. & Clin. Med., September, 1939, 24: 1310.*—(*F. G. P.*)

Tubercle Bacilli in Tuberculosis of Skin.—In 18 cases of lupus vulgaris, 16 positive guinea pig inoculations were obtained, one was negative and in one the animal died intercurrently. From these 16 positive inoculations 15 culture strains from the organs were obtained, 10 showing human type tubercle bacilli, one attenuated bovine, and in 4 the type could not be ascertained. In 3 cases of *tuberculosis verrucosa cutis* one human, one bovine and one undetermined type were recovered. In 2 cases of *scrofuloderma* bovine type bacilli were obtained. The cases of *erythema induratum* and papulonecrotic tuberculides gave negative results on guinea pig inoculation. The 20 per cent incidence of bovine type bacilli is considered of definite significance and would probably be increased with further research facilities.—*Researches on the Types of Tuberculous Bacilli in Skin Tuberculosis and Especially in Lupus Vulgaris, J. Kamienski, Tubercle, October, 1939, 21: 17.*—(*A. P.*)

Antigenic Differences of Avian Tubercle Bacilli.—Rabbit antiserum was prepared against 6 different strains of avian tubercle bacilli. Four of these strains were studied in their associated condition, while 2 of the cultures were dissociated into R and S variants. By means of direct agglutination tests it was found that the cultures fell into 2 distinct antigenic groups and that the anti-S and anti-R sera were specific. By means of absorption experiments differences in antigenicity of the strains could be demonstrated. Antigenic differences could be demonstrated between the anti-R and anti-S variants. Although the S variant absorbed the anti-R immune bodies, the reverse was not true. In general the S variant produced a flaky agglutination, while the R variant produced a granular agglutination. However, with some strains a flaky granular reaction was observed. The author confirms the studies of previous investigators in finding that there are several subgroups of avian tubercle bacilli.—*Versuche einer Differenzierung der säurefesten Bakterien mittels des Agglutinationsverfahrens, G. Abel, Zentralbl. f. Bakt., December, 1939, 145: 126.*—(*J. D. A.*)

Types of Tubercle Bacilli in Renal Tuberculosis.—The types of tubercle bacilli found in 55 cases of renal tuberculosis and in one case of tuberculosis of the testes are discussed. Identification of type was based on size, shape, color and rate of growth of colonies, microscopical appearance of the organisms and their pathogenicity for rabbits and guinea pigs. In a series of 63 tuberculous abscesses found in 36 kidneys the author found human as well as bovine type bacilli in the softened areas and in the abscess walls. The more liquid the contents of these abscesses, the greater the preponderance of human over the bovine type. This is explained by the fact that while the bovine type multiplies in man it brings about a cellular infiltration, but no tubercle formation. Acid-fast bacilli are not demonstrable in these lesions, but clumps of acid-fast granules and non-acid-fast bacillary bodies are present. These changes in the morphology of the tubercle bacilli are brought about by phagocytosis and other immunobiological processes. On the other hand, it is claimed that the human type resists such processes at first, but is ultimately destroyed, as evidenced by the fact that the pus from these abscesses is frequently found to be sterile. Caseation is not brought about by leucocytic enzymes, but by the metabolic products of the tubercle bacillus; on the other hand, softening is due to the leucocytic enzymes. From 16 ulcerated papillomata, 15 cultures of tubercle bacilli were isolated. Of these, 9 proved to be bovine, and 3 were classified as human, despite their marked pathogenicity for rabbits,

which was attributed by the authors to the presence of some bovine type organisms. From 44 tubercles 32 cultures were obtained; 19 were classified as human type, 9 as bovine and 4 atypical. In every instance the human types were found to be mixed with bovine tubercle bacilli. From 5 cases of infarct of the kidneys 4 atypical cultures were isolated. The authors state that in the giant cells of these tubercles the bacilli frequently occurred in pairs. In their opinion one of the organisms was human, while the other was bovine. From 6 cases of tuberculous pyelitis they isolated one human strain, 2 bovine and 3 atypical strains. They conclude that bovine as well as human type tubercle bacilli are essential for the development of tubercles and that bovine bacilli induce only a cellular infiltration and cannot produce tubercles.—*Bakteriologische Typenuntersuchungen in histologischen Präparaten bei Nierentuberkulose, E. Groh & T. Remete, Zentralbl. f. Bakt., October, 1939, 144: 495.—(J. D. A.)*

Saprophytic Acid-fast Bacilli.—One hundred and thirty strains of acid-fast saprophytic bacilli were isolated in the years 1932 to 1936 from 26,343 specimens of human material examined at the State Serum Institute. Fifty-eight per cent of the 130 strains were isolated from stomach washings, 18 per cent from urine and 10 per cent from sputum specimens. Two improvements in technique increased the number of strains found. The culture medium was changed from Petroff's to an egg-asparagin medium with .75 per cent glycerine, and 6 per cent sulphuric acid was used instead of sodium hydroxide for homogenization. Three procedures were used to distinguish saprophytic organisms from tubercle bacilli: (1) prolonged observation of the primary culture; (2) subculture on solid egg medium and in Besredka's fluid medium, and (3) intracutaneous inoculation into guinea pigs. Fifty-five of the 130 strains had bright orange colonies. None of the strains was pathogenic for guinea pigs; only local lesions were formed which healed promptly. The ability to cause a local lesion was limited almost entirely to the most dysgonic strains with orange pigment.—*Saprophytic Acid-fast Bacilli as a Source of Error in Diagnostic Work, Vera Lester, Acta tuberc. Scandinav., 1939, Fasc. 3–4, 13: 251.—(H. R. G.)*

Allergy and Immunity.—Forty-eight albino guinea pigs were divided in two equal groups and kept in a room with the temperature constant at 15 to 17°C. A normal desensitized group averaged 639 g. in weight and a normal control group 653. One week before infection subcutaneous injections of 100 mg. of Old Tuberculin was begun on the normal desensitized group and continued throughout the experiment on a thrice weekly schedule. All animals were infected subcutaneously in the left groin with 0.02 mg. of virulent bovine tubercle bacilli of strain Laporte 815-3. Tuberculin tests with 10 mg. of Old Tuberculin were made on both groups at five intervals, the last on the 140th day of infection. The normal desensitized group averaged 21 per cent positive with an average reaction volume of 510 cm. The normal control group were 100 per cent positive with an average reaction volume of 2772 cm. The average weight curves rose until about the twenty-fifth day, and then gradually declined, the weight reaching about 540 g. at the end of the experiment. The normal desensitized group showed statistically significantly less tuberculous involvement pathologically and by comparing the weights of the lymph nodes, spleens, and lungs. Comparisons with the work of Willis and coworkers are made.—*Allergy and Immunity (Iathergy) in Experimental Tuberculosis. IV. Degree of Tuberculosis in Guinea Pigs Prevented from Becoming Tuberculin Hypersensitive, K. Birkhaug, Acta tuberc. Scandinav., 1939, Fasc. 3–4, 13: 221.—(H. R. G.)*

Allergy and Immunity.—From previous studies in Skandinavian children and nurses the conclusion cannot be made that tuberculin allergy is associated with tuberculosis immunity. On the contrary, the primary infection probably diminishes the resistance of the organism against tuberculosis. The original theoretical grounds for BCG vaccination as a protection against tuberculosis infec-

tion are dubious. The conclusions of the author are based on the literature discussed and not on investigations of his own.—*Ist positive Tuberkulinreaktion ein Zeichen von Tuberkuloseimmunität? Mit besonderer Berücksichtigung der Untersuchung an Krankenpflegepersonal, O. Ljung, Ztschr. f. Tuberk., September, 1939, 83: 1.*—(*G. C. L.*)

Vaccination against Tuberculosis.—The virulence of tubercle bacilli was modified by the addition of an antiserum prepared by injecting rabbits with a mixture of old tuberculin and diphtheria anatoxin. The author believes that this antiserum injures the cell membrane, permitting the escape of the antigen. The effects of such a vaccine on guinea pigs were studied. A first vaccine was prepared by heating an emulsion of a three weeks old virulent culture of human bacilli and the antiserum for forty minutes at 55°C. The guinea pigs received 10 mg. of this culture and 2 cc. of the antiserum. This vaccine was found to be sterile, and upon microscopical examination the organisms were found to be diphtheroid in appearance. Two weeks following the injection of the vaccine a nodule developed at the site of injection and the regional lymph nodes were enlarged. The nodules and lymph nodes increased in size for six weeks, when they began to regress and finally resumed their normal size. These animals were next injected with 1.5 cc. of antiserum and 10 mg. culture heated at 50°C. for forty minutes. Two weeks later a small nodule was noted at the site of injection, which by the end of five weeks had grown larger, while the regional lymph nodes were but slightly enlarged. The local swelling and enlarged nodes began to regress in 7 animals six weeks after injection, while in 3 animals the lesions progressed and the animals ultimately died from tuberculosis. The surviving 7 guinea pigs were again injected with 5 mg. of vaccine, prepared by heating the culture for forty minutes, at a temperature of 45°C., with 1.0 cc. of the antiserum. The results were in accord with those previously observed. Four of these pigs were now injected, with a vaccine prepared by heating the culture for ten minutes at 40°C. with 1.0 cc. of the antiserum. A rise of temperature up to 1.0°C. was observed eight to twenty-four hours later. A swelling appeared two weeks after inoculation at the site of injection, and in the enlarged lymph nodes occasional alcohol-fast bacilli were found. At the site of injection a sinus developed. Three of the animals subsequently died from tuberculosis and one from an intercurrent disease. Three of the previously vaccinated animals received a vaccine of 5 mg. of an unheated culture of tubercle bacillus and 2.0 cc. of the antiserum. The injection was followed by a slight rise of temperature eight to twenty-four hours later. These animals developed a lesion at the site of injection and ultimately died from tuberculosis. As control normal rabbit serum was used with a vaccine prepared by heating a strain of virulent tubercle bacilli at 55°C. for forty minutes. These guinea pigs died in three to four months from extensive tuberculosis. Guinea pigs vaccinated with BCG all survived. The author concludes that the antiserum possesses bacteriolytic properties, and that the heated tubercle bacilli produce well marked local reactions due to the attenuated tubercle bacilli. Immunity is evidenced by the increased length of life following the last injection of tubercle bacilli. A vaccine prepared from the BCG culture and the antiserum gave definite protection in guinea pigs. In man it would be advisable to vaccinate first with BCG, followed by the bovine type, and finally with a human type culture, while in cattle vaccination should begin with the human type followed by BCG and conclude with the bovine type.—*Versuche zu einer simultanen Vakzination gegen Tuberkulose, N. Nikolić, Zentralbl. f. Bakt., November, 1939, 145: 31.*—(*J. D. A.*)

BCG Vaccination.—Clinical and experimental studies during the last fifteen years have now made it possible to form certain definite conclusions regarding vaccination with BCG. Vaccination with BCG is absolutely harmless. All harmful clinical results, such as the Lübeck disaster, have been proved to have been the result of accident. Moreover, it has been impossible, experimentally, to convert BCG into a virulent organism. The efficacy of BCG has been demonstrated

without question. Experimentally, it has been possible to protect cattle, monkeys and rabbits against a virulent inoculation of tubercle bacilli. In the guinea pig, the survival time has been prolonged and the infection takes a different course with the formation of pulmonary cavities. Clinical studies have manifested similar favorable results. The immunity conferred by the BCG vaccination is only relative and is rather weak; it is in no way comparable to the immunity conferred by inoculation for diphtheria or tetanus. When infants, successfully vaccinated with BCG, are exposed to any sort of massive tuberculosis, they will develop and frequently succumb to the disease. While vaccination can undoubtedly be carried out by the oral route, the parenteral method is more exact and more successful. The usual dose is .01 mg. in 1 cc. The author prefers the scarification method. It can be administered by injection into the lumbar region or by the multiple puncture method. The reactions are minimal and practically never of any significance. It is possible to render 100 per cent of the vaccinated infants tuberculin-positive. The tuberculin test should be carried out from six to eight weeks after vaccination. In the rare cases, in which the tuberculin test is negative, revaccination should be carried out. During the first two years of life, exposure to tuberculosis is usually familial and massive. BCG vaccination is of little value against such infections. Consequently, during this period, strict isolation of the infant is of greatest value. After the first two years of life, the value of vaccination increases. Not only should young children be vaccinated but also all tuberculin-negative adolescents and young adults, particularly medical and nursing students who come into particular contact with the disease.—*Indications et technique de la vaccination par le BCG, J. Paraf, Progrès méd., January 6, 1940, 68: 21.*—(*H. R. N.*)

Allergy and Immunity in BCG Vaccination.—The author has noted that in families with open tuberculosis the vaccinated children are frequently tuberculin-negative while the unvaccinated children are tuberculin-positive. Histories are given of 16 households in which these circumstances were observed. There were 11 unvaccinated children; all reacted to tuberculin and had tuberculous lesions demonstrable by X-ray examination. There were 30 children who had been vaccinated, usually by mouth, shortly after birth; none reacted to doses as high as 10 mg. OT when tested at the ages of two to nine years. In spite of the prolonged exposure to infection, no vaccinated child in these households died of tuberculosis. Revaccination with BCG, either by mouth or by subcutaneous injection, was attempted in the majority of these anergic children. A Koch phenomenon was observed in 2 instances. In each of these children, less than two years had elapsed since the first vaccination. In the other revaccinated children, tuberculin sensitivity developed to a slight degree or not at all. The sensitivity in those children who became tuberculin-positive was transient. Further attempts at vaccination resulted in feebler and more transient reactions. The importance of these observations in demonstrating the independence of immunity from allergy is emphasized. Experimental findings of other workers are cited to support the conclusion that the resistance of an organism to tuberculosis appears to increase in proportion to the number of benign infections that the organism has been able to overcome. The author points out also that his observations confirm the value of oral vaccination, and that this method should not be discarded merely because a large proportion of infants so treated failed to develop tuberculin sensitivity.—*Allergie et prémunition dans la vaccination par le BCG. Nouveaux arguments en faveur de l'efficacité de la méthode de vaccination de Calmette et Guérin, R. Chaussinaud, Rev. de la tuberc., 1939-1940, no. 8, 5: 916.*—(*H. L. I.*)

Tubercle Bacilli in Vaseline Oil.—Guinea pigs treated with killed bovine tubercle bacilli (S22) in vaseline oil show a greater tuberculin sensitivity than those treated with killed tubercle bacilli in saline. When these animals were infected six weeks later it was found that the immunity produced by the injection of killed tubercle bacilli in vaseline oil was better than that in the animals treated with killed

tubercle bacilli, but this immunity is erratic and is less successful than found in animals infected with live, attenuated tubercle bacilli. There was, however, a definite delay in the spread of infecting tubercle bacilli in the animals immunized with killed tubercle bacilli in vaseline oil.—*Über die Ausbreitungsgeschwindigkeit intrakutan verimpfter Tuberkelbazillen im Körper von Meerschweinchen, die mit abgetöteten Bazillen in Vaselinöl vorbehandelt waren, E. Haefliger, Ztschr. f. Tuberk., April, 1939, 82: 91.*—(*A. B. C.*)

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H. L. I.: Harold L. Israel, Philadelphia, Pennsylvania.
H. R. G.: Horace R. Getz, Philadelphia, Pennsylvania.
H. R. N.: H. R. Nayer, New York City.
J. D. A.: Joseph D. Aronson, Philadelphia, Pennsylvania.
J. S. W.: J. Stanley Woolley, Liberty, New York.
L. F. B.: Lauren F. Busby, Northville, Michigan.
M. A. B.: Morris A. Brand, New York City.
M. B.: Miriam Brailey, Baltimore, Maryland.
M. T. W.: Mildred T. Woolley, Charleston, West Virginia.
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